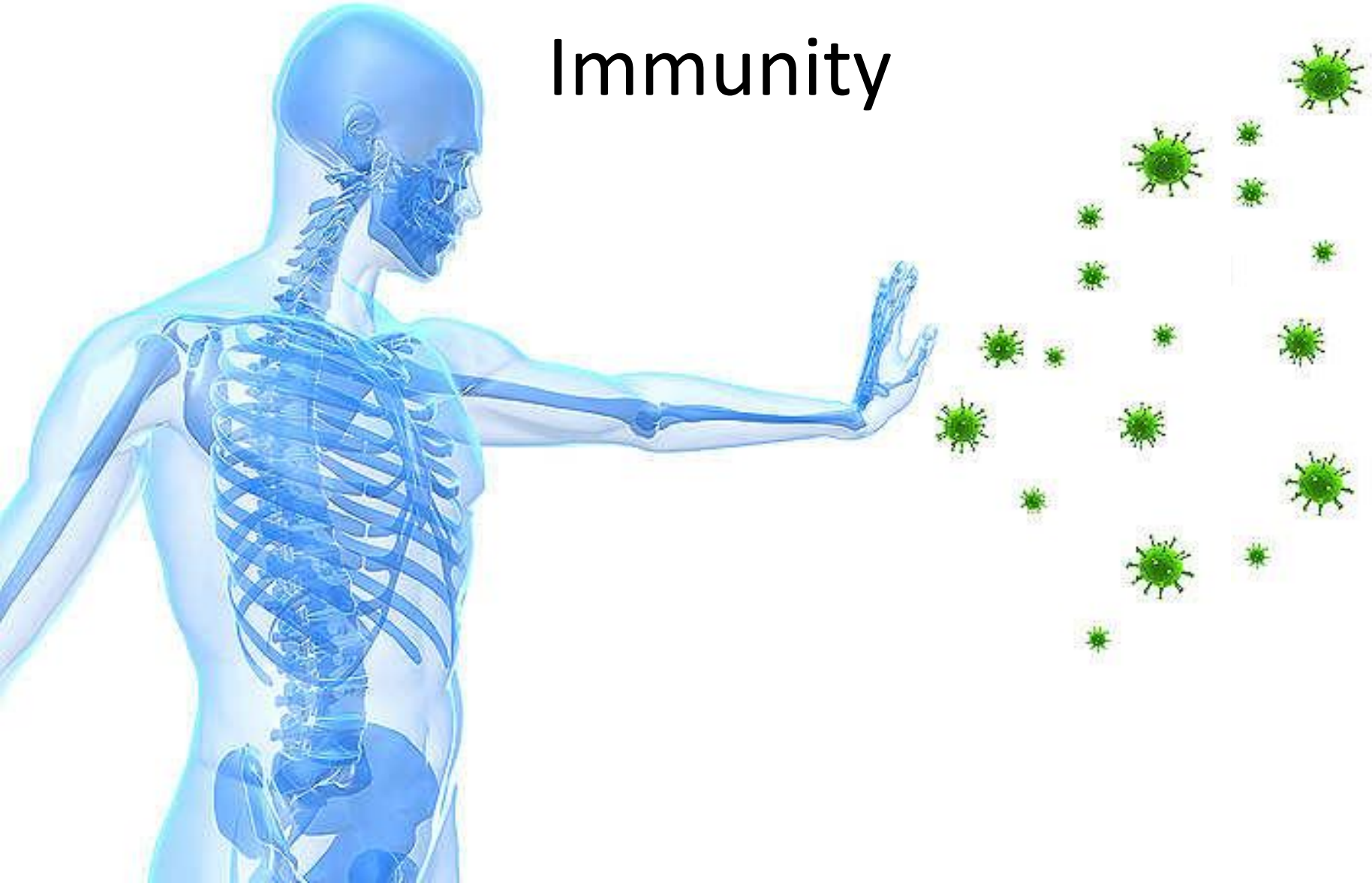
Cambridge Assessment International Education

AS Level
Chapter 11

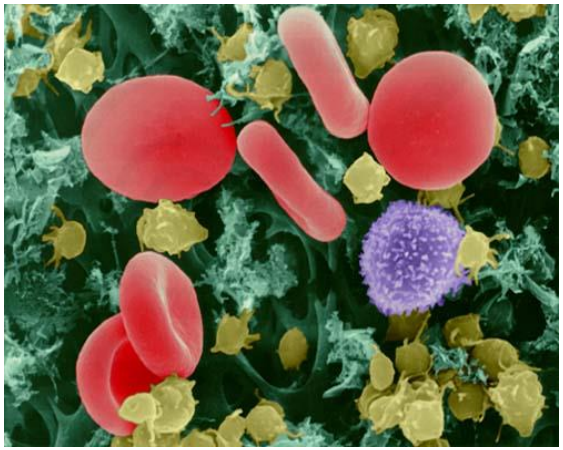
Immunity



Chapter Outline

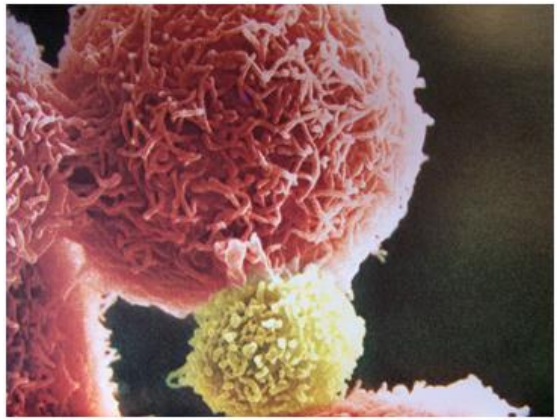
Part 1: The Immune Response

- Definitions: Immune response, antigen, self and non-self
- **Phagocytes**
  - Antigen presentation
- **B-lymphocytes**
  - Antibodies: structure and function
  - plasma cells and memory cells
- **T-lymphocytes**
  - T helper cells and T killer cells



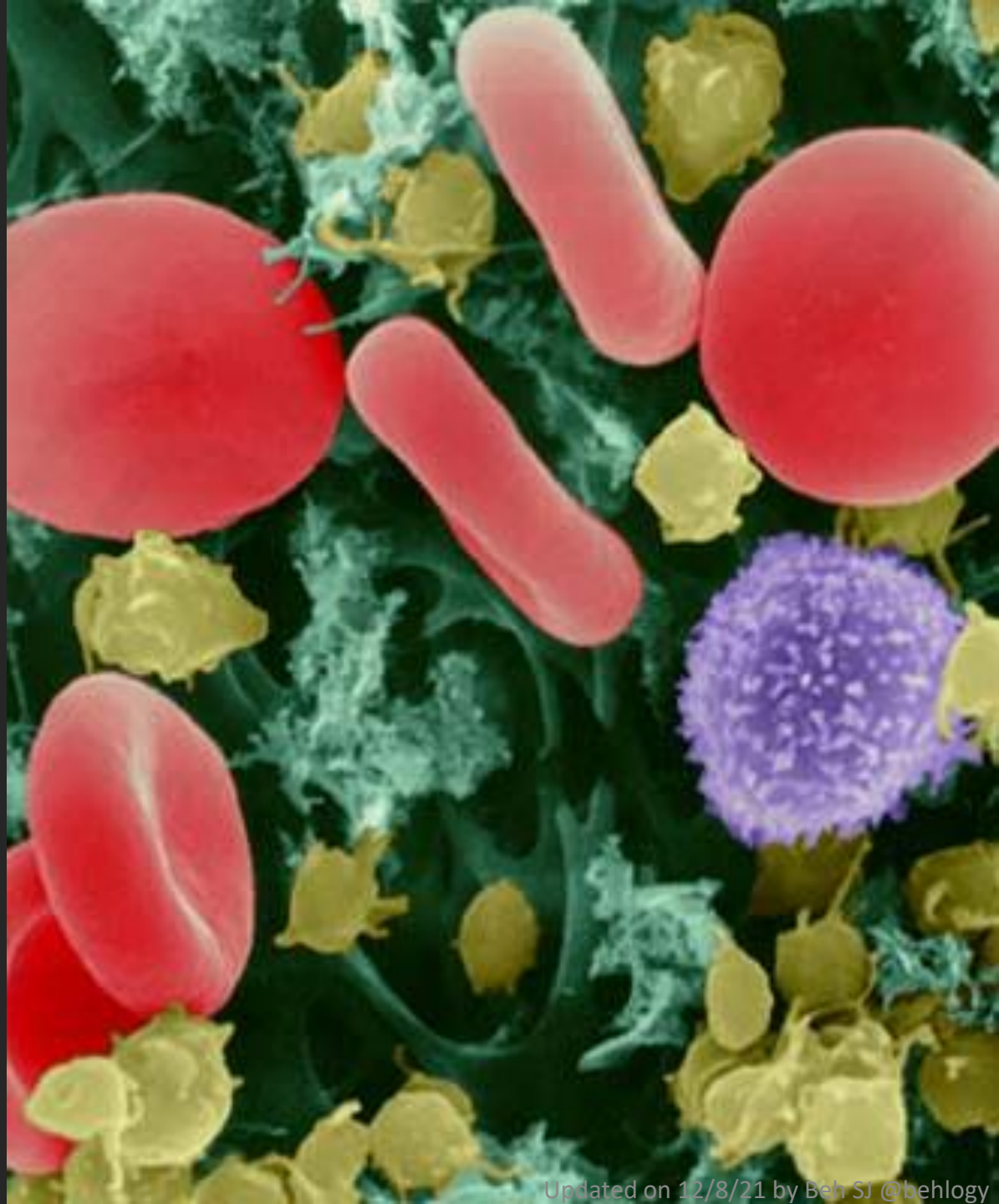
Part 2: Vaccination and Monoclonal Antibodies

- Active vs Passive // Natural vs Artificial Immunity
- **Vaccination**
  - How smallpox was eradicated
  - Why vaccines aren't effective for other diseases
- **Monoclonal antibodies**



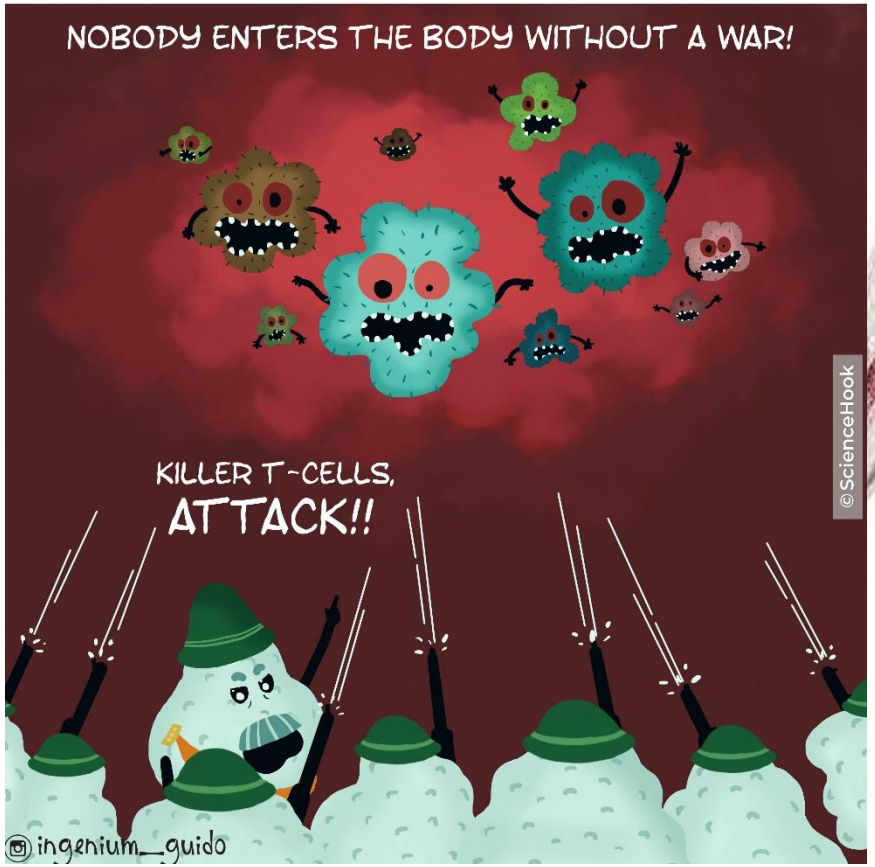
Chapter 11 (Part 1)

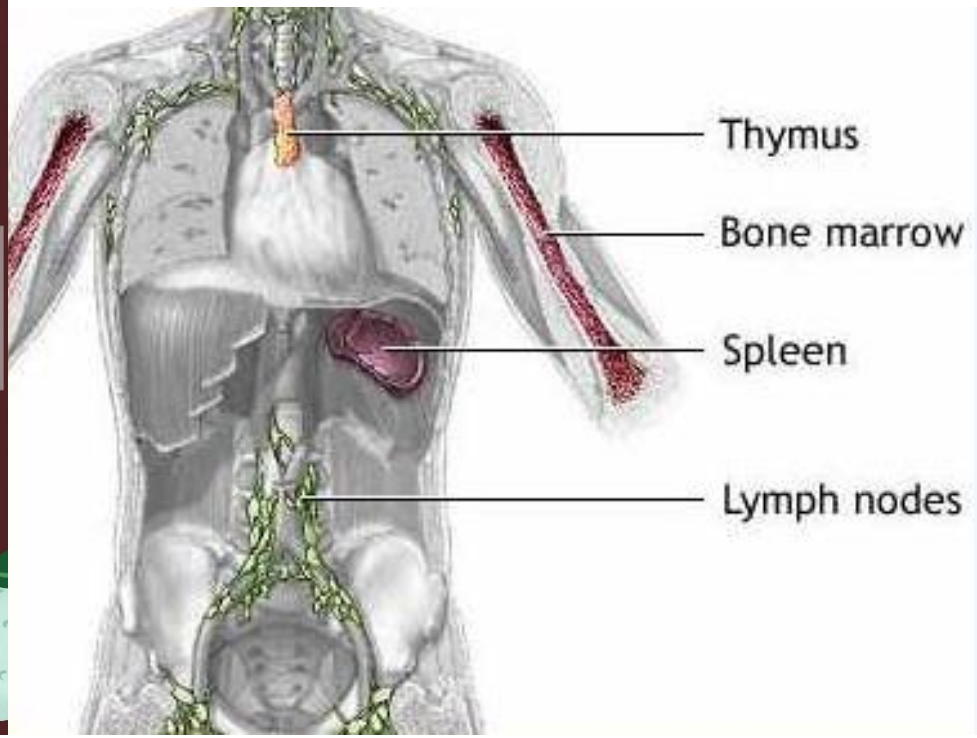
The Immune Response



Definitions

- Immunity = Protection against diseases
- Immune system = The body's defense system





Lines of Defences Against Diseases

- To prevent infectious diseases from entering and spreading

1) First line of defence

- External, **non-specific**

2) Second line of defence

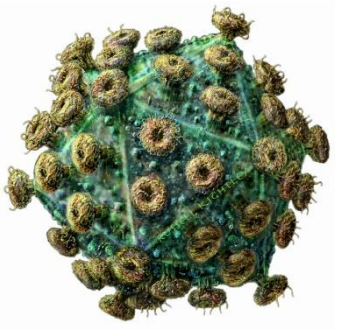
- Internal, **non-specific** immune response
- Involves **phagocytes**

3) Third line of defence

- Internal, **specific** immune response
- Involves **lymphocytes**

- Both non-specific and specific defences work together to protect the body against diseases

Definitions



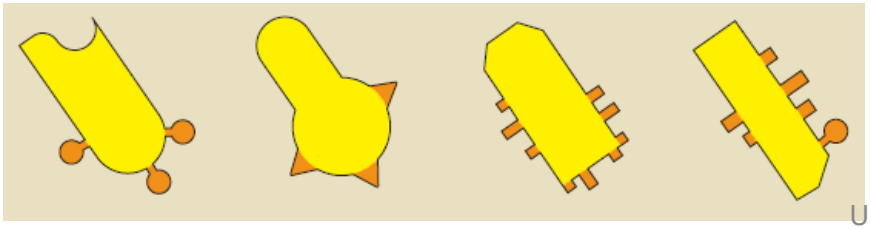
- **Antigens**
- 2 types: Self and Non-self
- In general, antigens are macromolecules on cell surfaces
- E.g. protein, glycoprotein, glycolipid, polysaccharides etc.

1) Non-self antigens = **macromolecules that activates an immune response**

- Macromolecules are found on…
  - **foreign materials'** surface (e.g. pathogen, allergen)
  - surface membrane of **infected host cells**

→ Stimulates production of antibodies

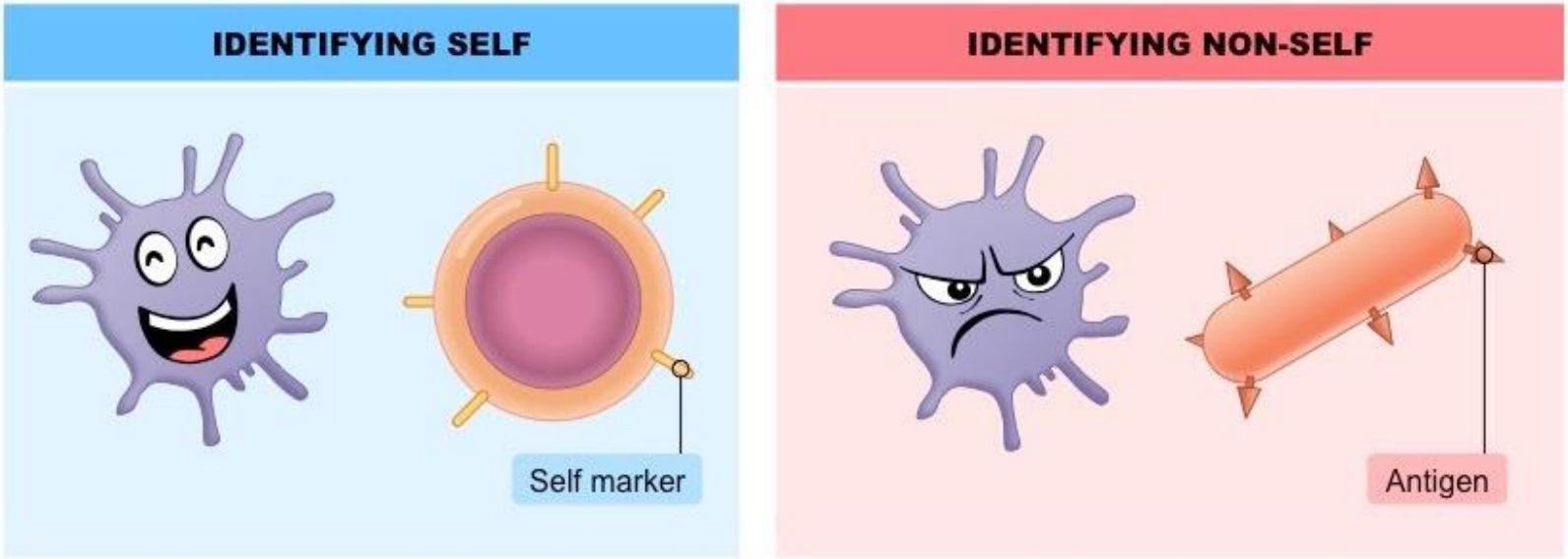
Representative diagram showing
diff antigens on surface of diff pathogen



Definitions

2) Self antigens / cell marker

- **Macromolecules on cell surface membranes** of host cells
- Cell surface antigens do **NOT** trigger body's immune system
- No antibodies are produced



Note: when we say antigen in general, we are usually referring to NON-self antigen though

Definitions

Immune response = the body's immune reaction towards **non-self antigens**

Involves WBCs that made in bone marrow (Chap 8)

1) Phagocytes

(mostly non-specific defence)

- Neutrophils
- Monocytes
  → which mature into macrophages

2) Lymphocytes

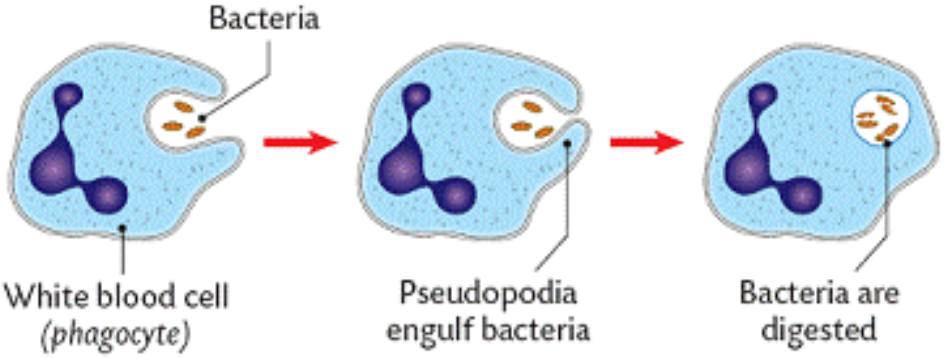
(mostly specific defence)

- B-lymphocytes
- T-lymphocytes

Chap 8 Recap

*yellow highlights = points important for this chap!

1) Phagocytes

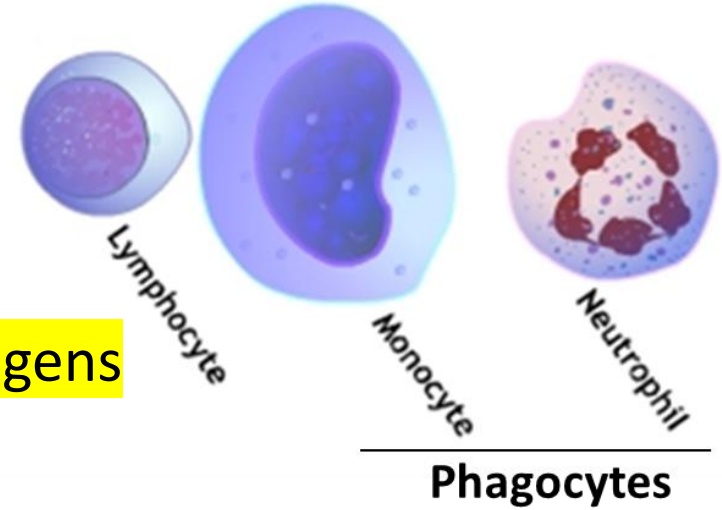


- Produced throughout life

Function:

- Patrol in blood, tissues and organs
- Remove dead cells and pathogens

→ By **phagocytosis** (Chap 4)



- Involved in **non-specific defense**

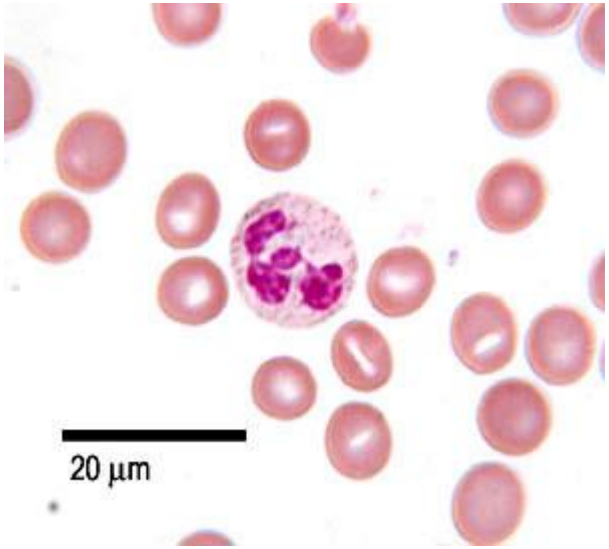
→ responds to many different non-self antigens

Appearance:

- **Lobed nuclei**
- **Granular cytoplasm** – due to many vesicles

Chap 8 Recap

1) Phagocytes



E.g. Neutrophils

- **Multi-lobed nucleus**
- Have **receptor proteins** on its membrane

→ **To identify pathogens as non-self**

- When there is an infection, large numbers are released from bone marrow

→ **Accumulate at site of infection**

- Short-lived (few hours-days)

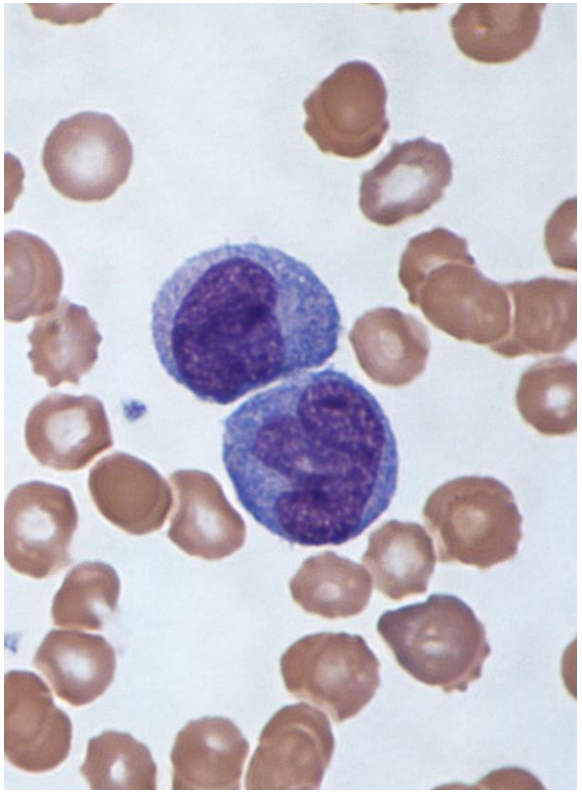
→ Dies after digesting pathogens

→ Dead neutrophils form pus :O

Updated on 12/8/21 by Beh SJ
@behlogy

Chap 8 Recap

1) Phagocytes



E.g. Monocyte → Macrophage

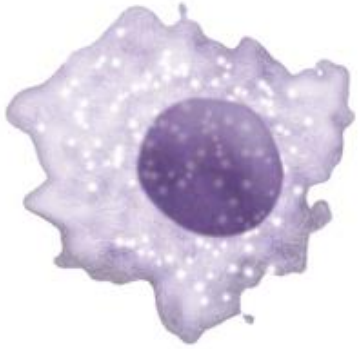
- **Lobed nucleus** / kidney-bean shaped
- Larger than neutrophils
- Have **receptor proteins** on its membrane

→ **To identify pathogens as non-self**

- Monocytes = circulate in blood

→ Mature into macrophages when it leaves blood and enter organs

Monocyte



Macrophage

- Long-lived cells
- Macrophages found in organs such as liver, lungs, spleen, kidney, lymph nodes

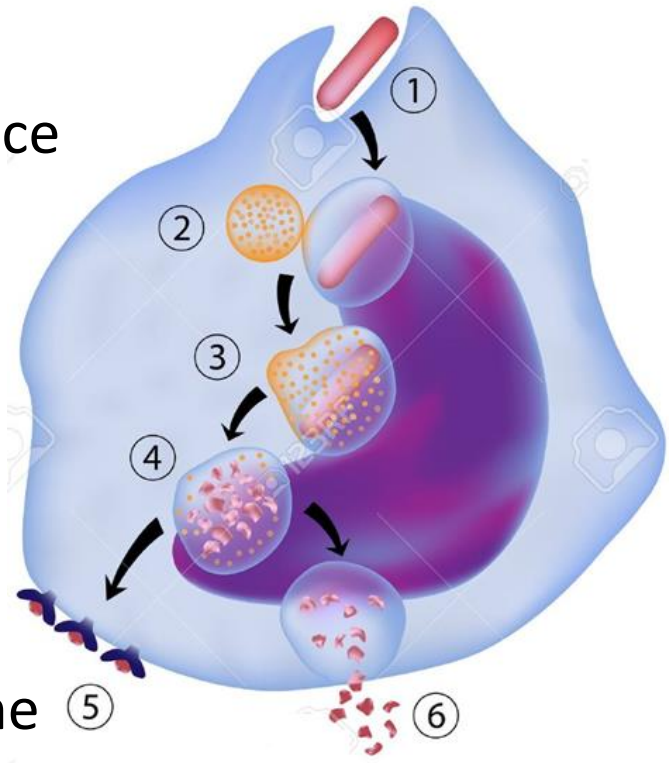
Updated on 12/8/21 by Beh SJ
@pehmgy

Role of Macrophages

- **Initiates / starts the immune response**

Mechanism:

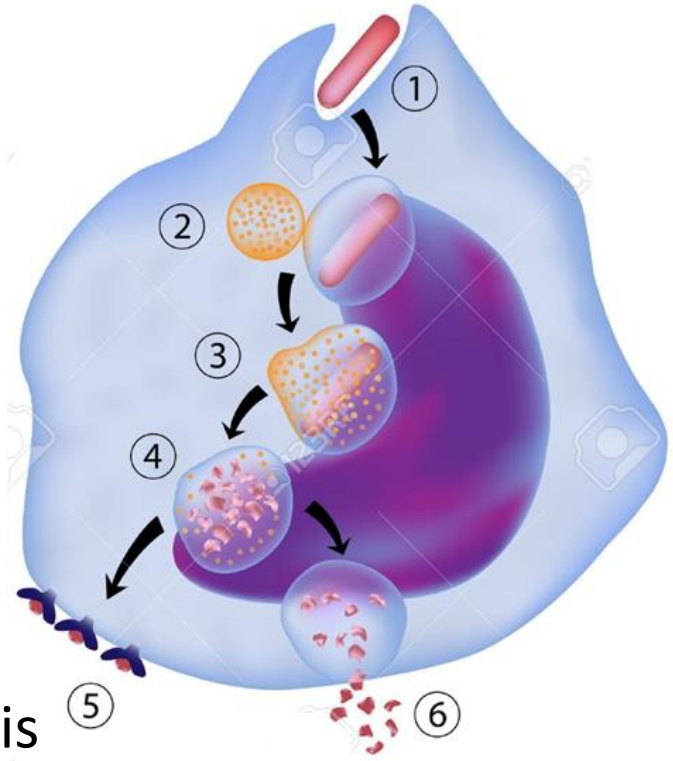
1) Has various **receptor proteins** of cell surface
- Can detect non-self antigens
- **Non-specific**



2) Engulf pathogen / foreign material via **phagocytosis** (Chap 4)
- Fusion of phagocytic vacuole with lysosome

Role of Macrophages

- **Initiates / starts the immune response**



Mechanism:

3+4) **Cuts up pathogen** using lysozymes

5) Antigens presented on its cell surface

→ Macrophages act as **antigen-presenting cells (APC)**

6) Some cell fragments released by exocytosis

- APCs can activate / stimulate lymphocytes

*P/S: other APCs can include **B cells** and other types of **phagocytes** too!*

Updated on 12/8/21 by Beh SJ
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2) Lymphocytes

- Produced in bone marrow before birth

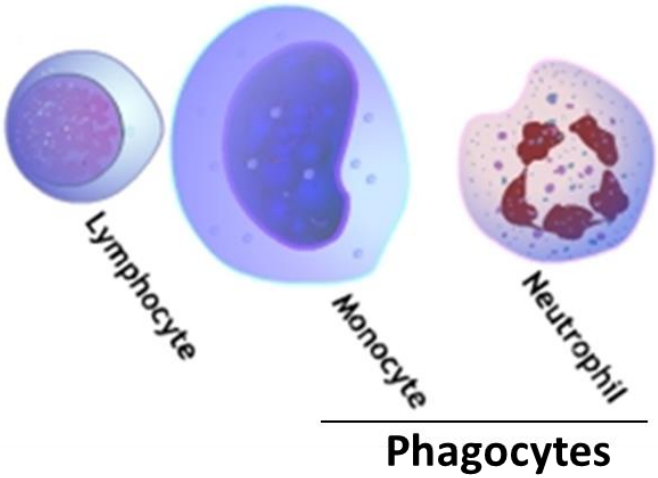
Function:

- Involved in **specific immune responses**

→ responds to only specific non-self antigens

- Mature lymphocytes circulate in the **blood and lymph**

→ **Accumulate at sites of infection**



Appearance:

- **Smaller** than phagocytes
- **Large round nucleus**
- **Little cytoplasm**

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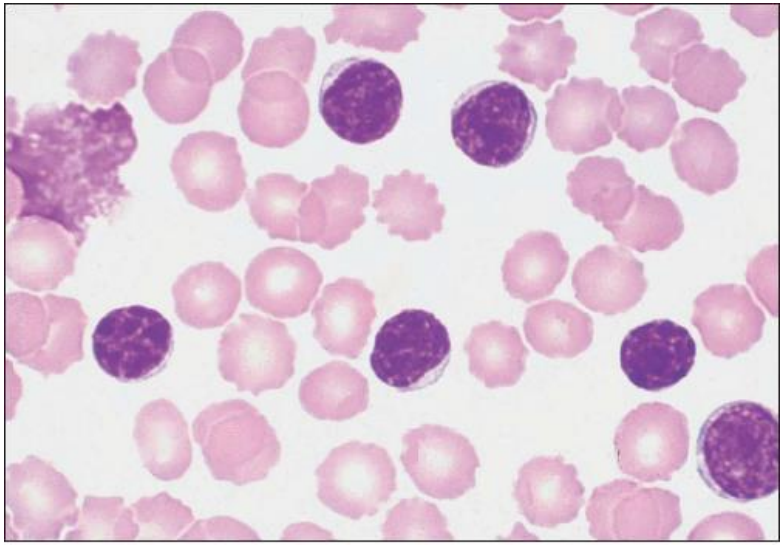
2) Lymphocytes

2 main types:

Both made in **bone marrow,** but mature in different places and have different functions

1. **B-lymphocytes (B cells)**
   - Mature in **bone marrow**
   - **Produces antibodies**

2. **T-lymphocytes (T cells)**
   - Mature in **thymus**
   - Does **NOT** produce antibodies



Source: Estella Matutes, Barbara J Bain, Andrew Wotherspoon
Lymphoid Malignancies: An Atlas of Investigation and Diagnosis
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- Both work together to defend the immune system

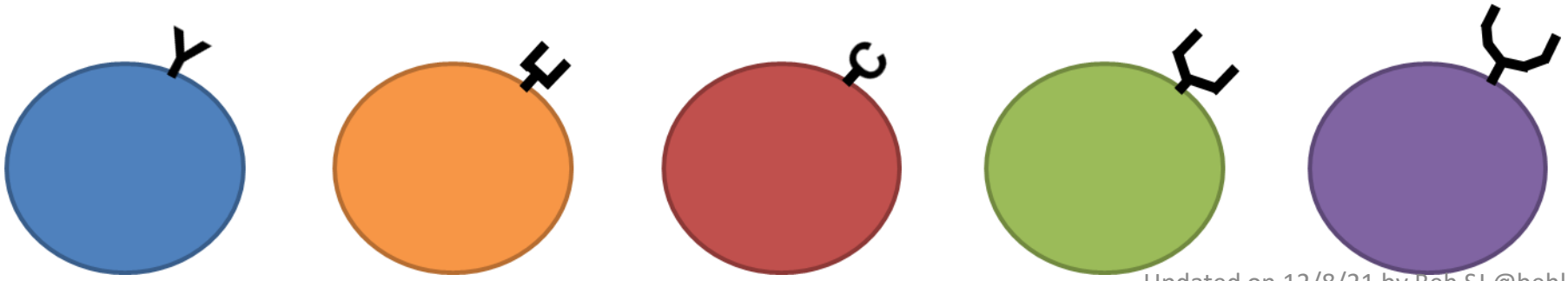
Lymphocytes

- Millions of different types of B and T-lymphocytes with receptors of different shapes
- **SPECIFIC = each type of lymphocyte responds to 1 type of antigen only**

E.g. Each type of **B cell** produce **1 type of antibody receptor**

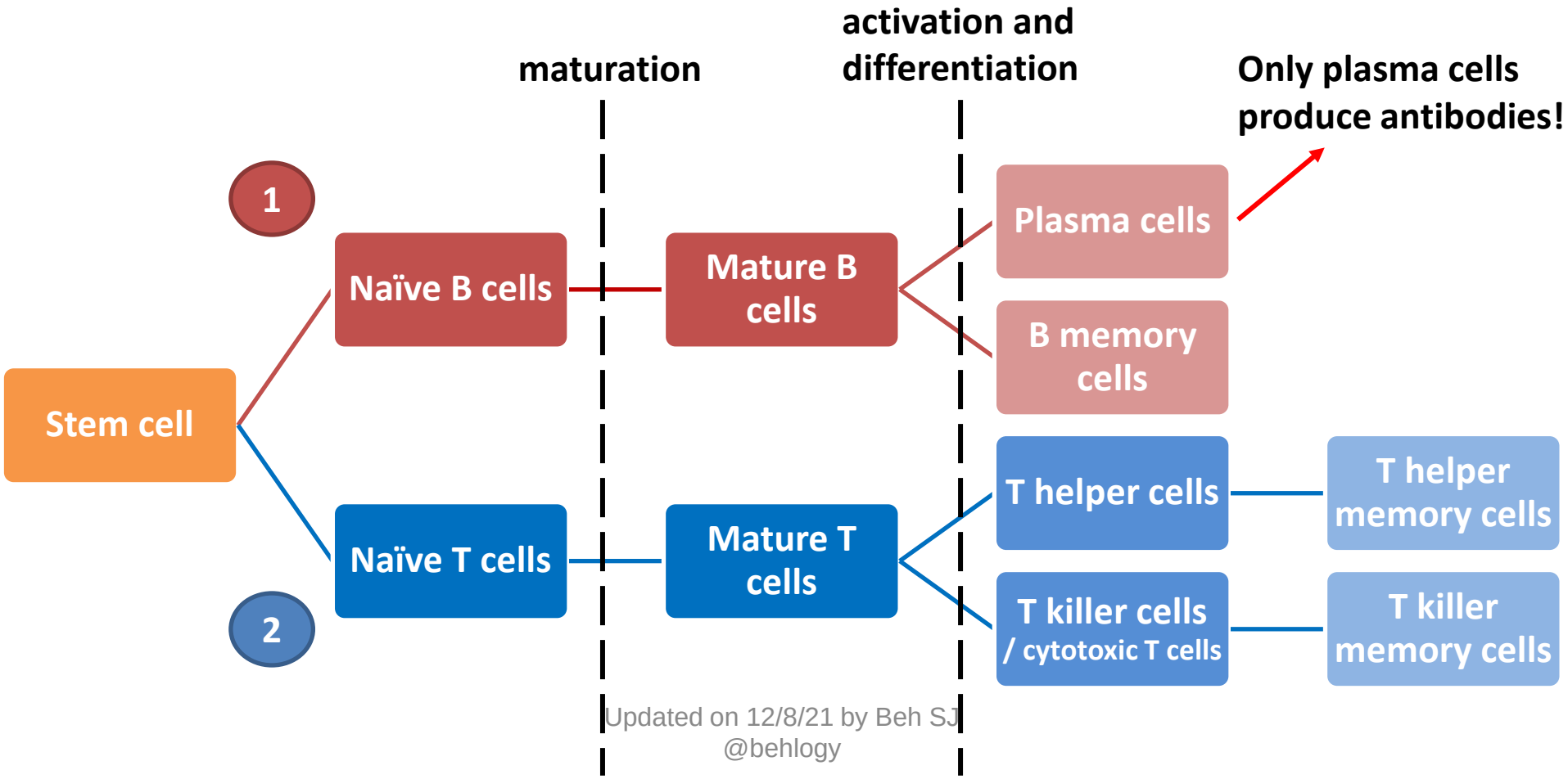
→ which responds to 1 type of antigen only

- So the body can respond to almost any type of pathogen



Lymphocytes

- Only **mature** lymphocytes can **circulate in the blood & lymph** and carry out immune responses
- Have **telomerase** to divide continuously



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Maturation of B-Lymphocytes

1) All B cells are **formed in the bone marrow before birth**

→ Genes in B cells that code for antibodies code for diff types of antibodies for diff types of B cells

2) Forms a **specific *antibody*** that acts as ***glycoprotein receptor*** **on surface membrane** of B cells

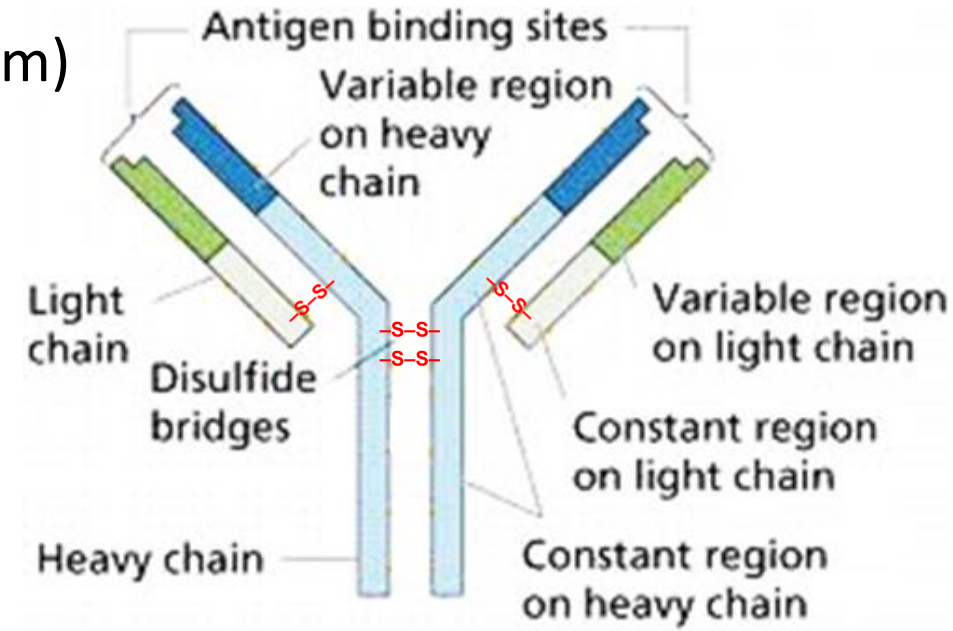
→Binds to **specific antigen that is complementary in shape**

3) B lymphocytes **divides and mature in bone marrow**

→ Mature B lymphocytes **circulate in blood** and **concentrate in liver, spleen & lymph nodes**

Antibodies

- Aka **immunoglobulins**
- **Globular glycoproteins**
  (carbo part not shown in diagram)



Made of 4 polypeptide chains:

- **2 heavy chains**
- **2 light chains**

→ Quaternary structure

- Held together by **disulfide bonds**

→ gives stability

1

Antibodies

Three regions:

1) Variable region (Fab)

- Every chain has a variable region = 4 in total
- Provide 2 identical **antigen-binding sites**

- **Specific** for binding antigen

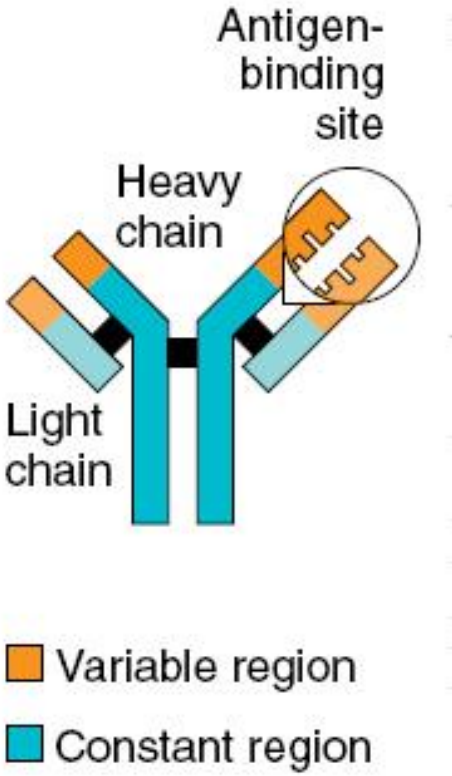
→ **Complementary shape to antigen**

→ Shape determined by primary structure = **specific seq of amino acids**

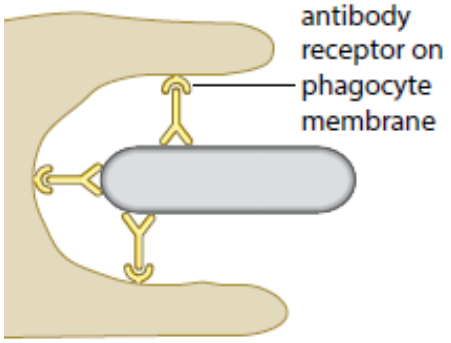
- R groups at antigen-binding site forms H bonds and ionic bonds with specific antigen

Sequence of amino acids at the variable region is different for each type of antibody

→ Each type of antibody binds different antigens

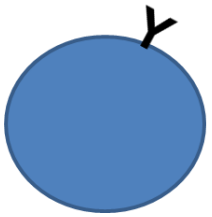


Antibodies



2) Constant region (Fc)

- Formed by light and heavy chains
- **When circulating in blood: binds to receptors on phagocytes**
- When antibody acts as B cell receptor: attach to cell surface membrane of B cell



- Gives antibody class

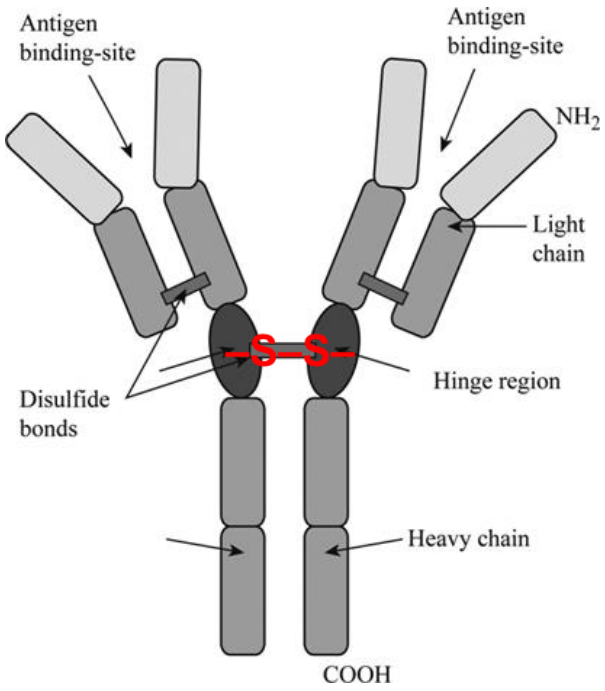
Aiyo no need to remember lah

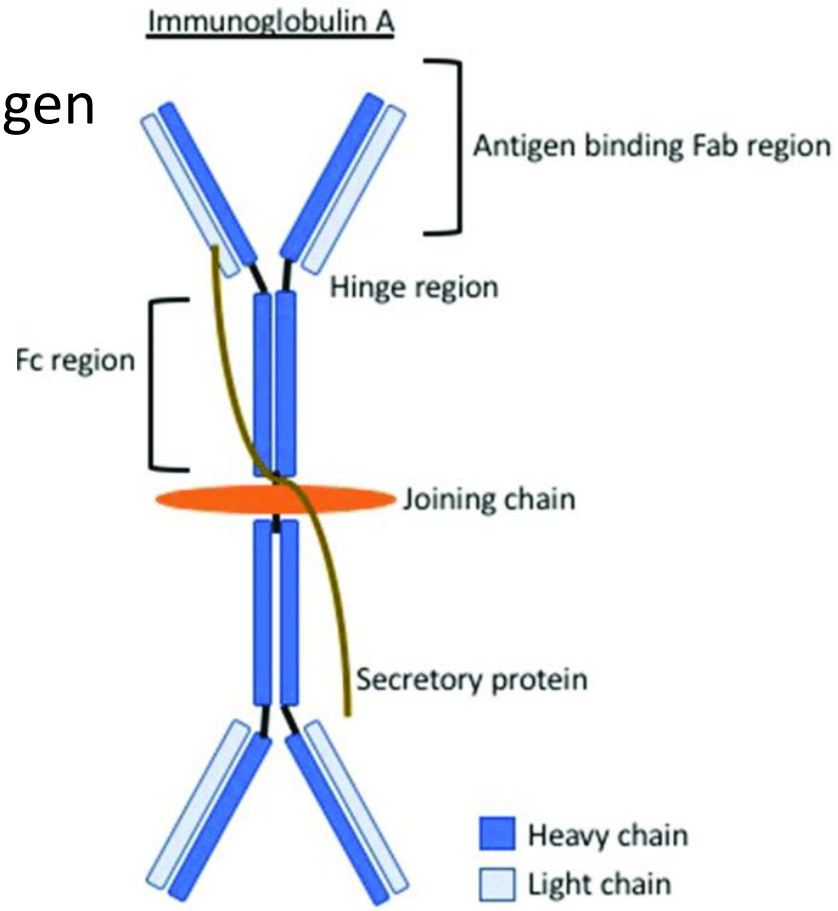
	IgM	IgG	IgA	IgE	IgD
Heavy Chain	μ (mu)	γ (gamma)	α (alpha)	ε (epsilon)	δ (delta)
MW (Da)	900k	150k	385k	200k	180k
% of total antibody in serum	6%	80%	13%	0.002%	1%

Antibodies

3) Hinge region

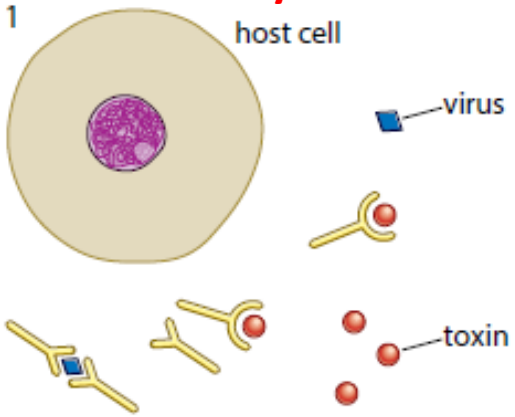
- Held by **disulfide bridges**
- **Gives flexibility** when binding to antigen





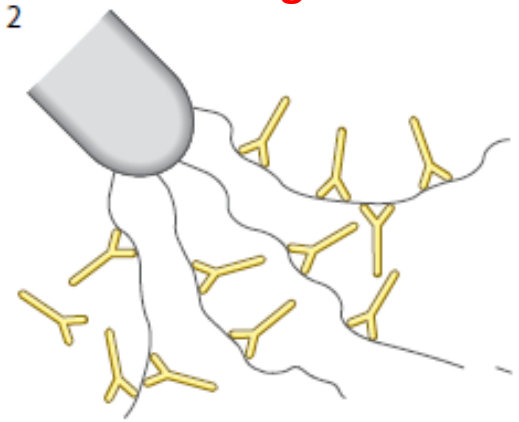
Action of Antibodies

Prevent entry into cell



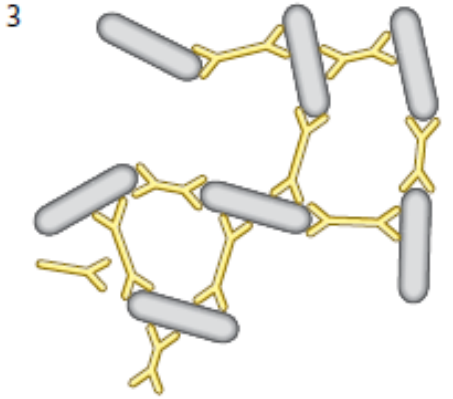
Antibodies combine with viruses and bacterial toxins preventing them entering or damaging cells.

Attach to flagella



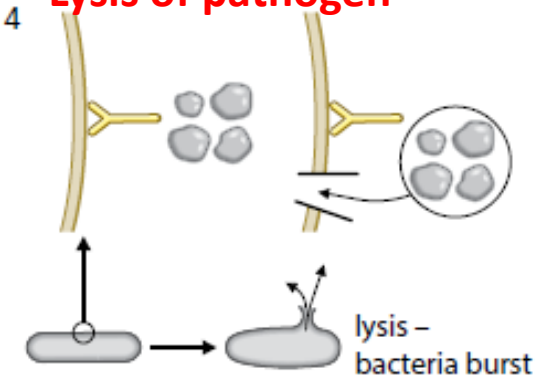
Antibodies attach to flagella of bacteria making them less active and easier for phagocytes to engulf.

Agglutination



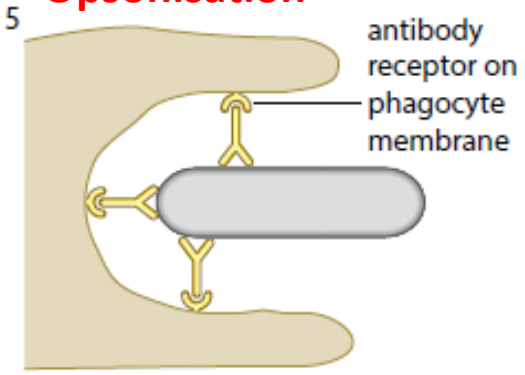
Antibodies with multiple antigen binding sites cause agglutination (clumping together) of bacteria reducing the chances of spread throughout the body.

Lysis of pathogen



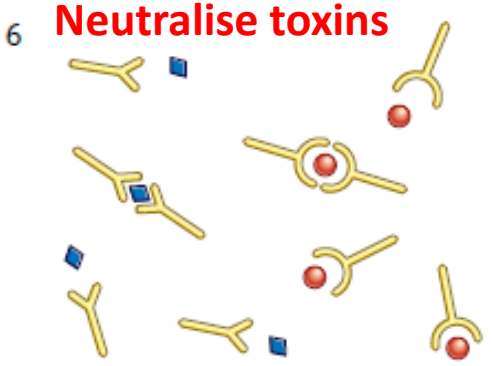
Together with other molecules, some antibodies 'punch' holes in the cell walls of bacteria, causing them to burst when they absorb water by osmosis.

Opsonisation



Antibodies coat bacteria, making it easier for phagocytes to ingest them; phagocytes have receptor proteins for the heavy polypeptide chains of antibodies.

Neutralise toxins



Antibodies combine with toxins, neutralising them and making them harmless; these antibodies are called antitoxins.

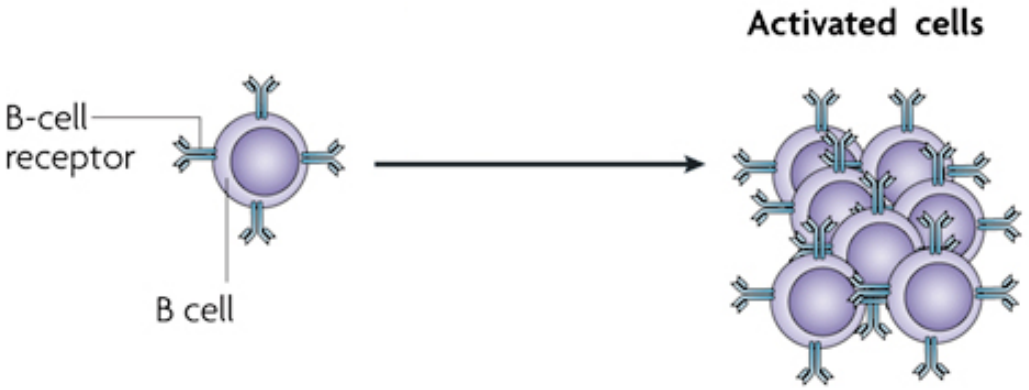
Action of B-Lymphocytes

1. Pathogens invade

2. **Antigen presentation cell** formation

3. **Only specific B lymphocytes has receptors with the complementary shape to antigen will be activated**
   → **Clonal selection**

4. B cell divides by **mitosis**
   → **Clonal expansion**



5. Activated B cells develop into **plasma cells** and **memory cells**

Plasma Cells

- **Short lived** (few weeks)
- Do not divide and do not have telomerase

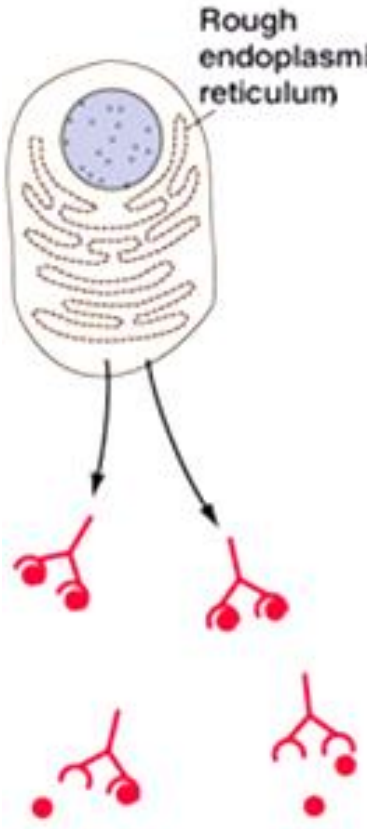
- **Produce and secrete antibodies** rapidly

→ by exocytosis

→ into blood plasma, lymph, lungs and stomach lining

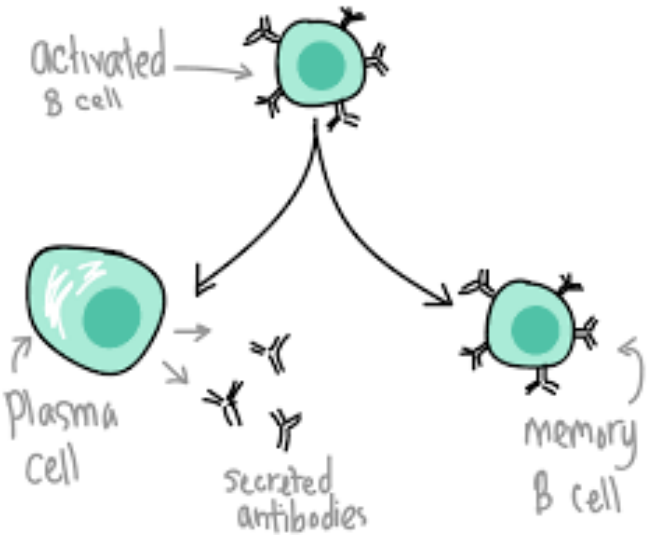
- Antibodies are glycoproteins

→ So plasma cells have extensive network of **RER and Golgi**



Memory Cells

- Long-lived, remain in circulation
- Has telomerase



- Provides **long term immunity**
- Last for many years/lifetime

- Enable **faster response** during
  2nd invasion of same antigen,
  as many memory cells are circulating

- During 2nd invasion, it divides rapidly (clonal expansion)

→ **Form more plasma cells → more antibodies**

→ Infection is destroyed before symptoms develop

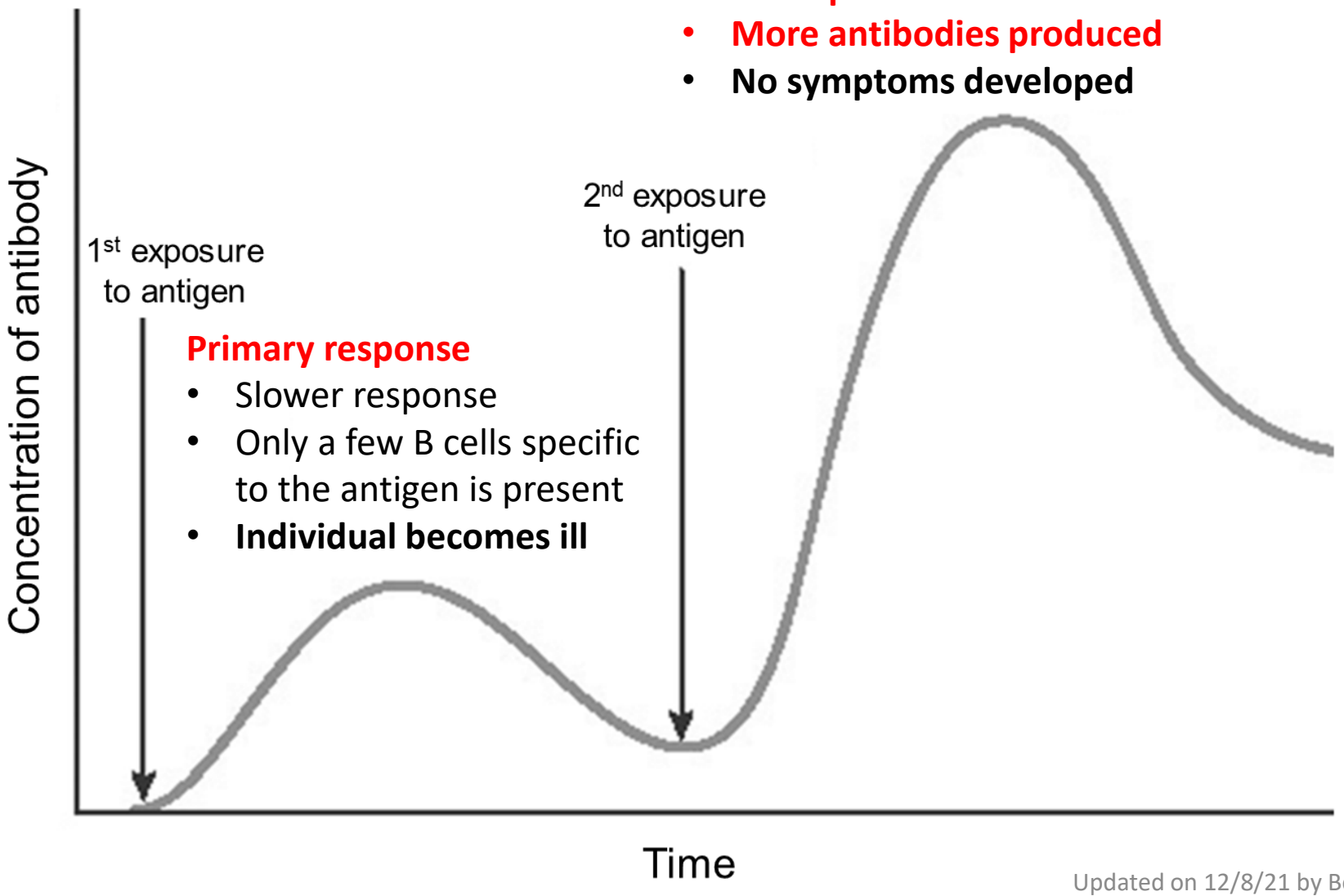
→ Body immune to pathogen

1

Memory cells

Secondary response

- **Faster response**
- Many memory cells circulating
- More cells specific for pathogen, higher chance of encountering pathogens quickly
- **More plasma cells formed**
- **More antibodies produced**
- **No symptoms developed**



Primary response

- Slower response
- Only a few B cells specific to the antigen is present
- **Individual becomes ill**

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Summary of Action by B-Lymphocytes

Bind with specific antigen on APC (Clonal selection)

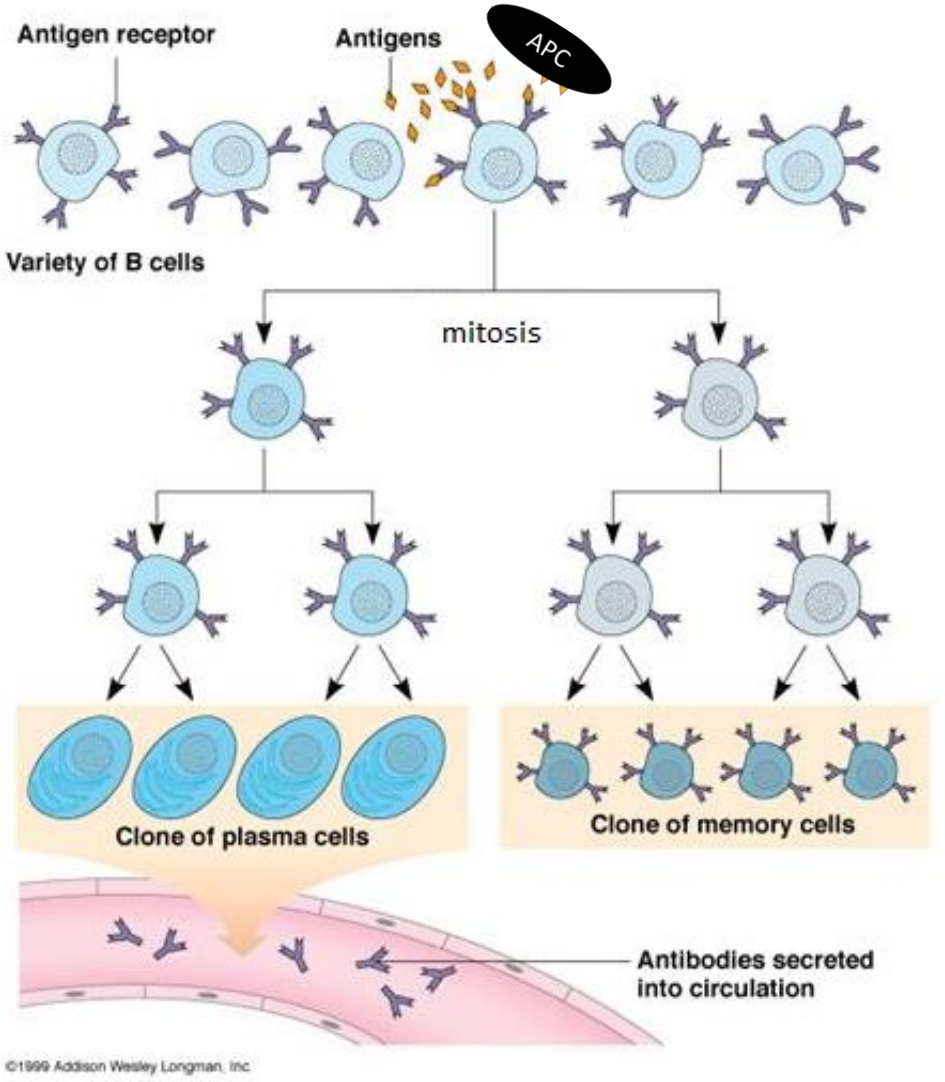
Divide by mitosis (Clonal expansion)

Formation of plasma cells

Formation of memory cells

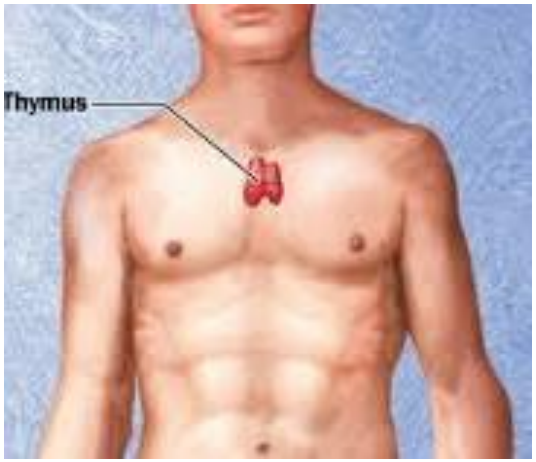
Production and secretion of antibodies

Enable faster response during 2nd invasion of same antigen



Maturation of T-Lymphocytes

1) All T cells produced in **bone marrow** before birth



2) Maturation in **thymus** gland

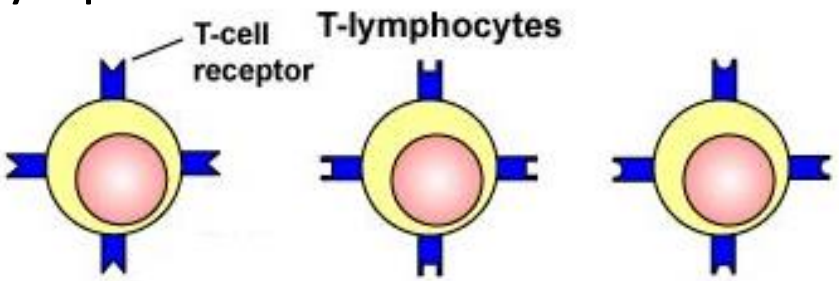
→ thymus shrinks after puberty

- Produce specific **T cell** receptors on cell surface membrane

→ Binds to **specific antigen that is complementary in shape**

→ T cell receptor's structure *similar* to antibodies

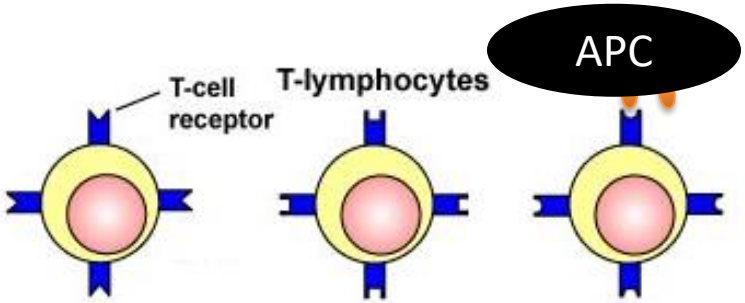
3) Mature T cells circulate in blood and lymph



Action of T-Lymphocytes

1. Pathogens invade

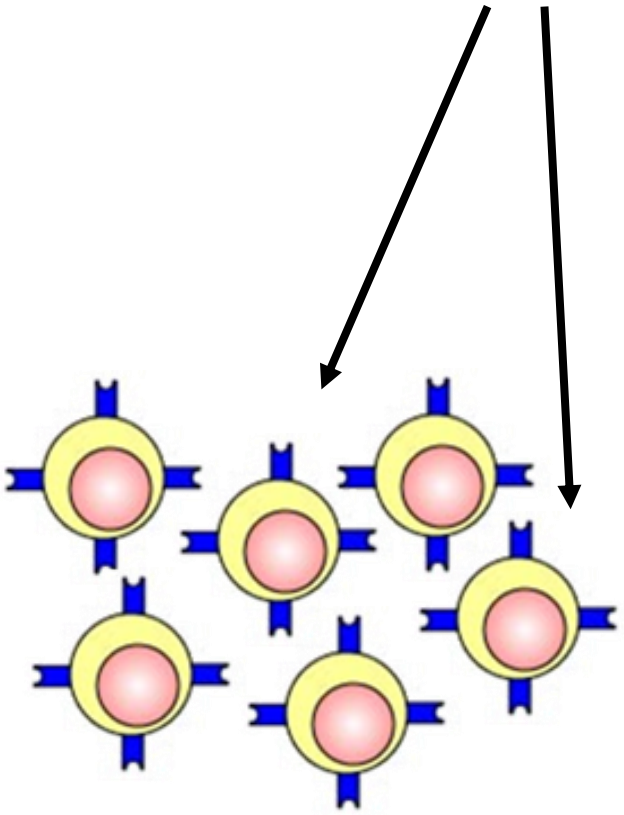
2. **Antigen presentation cell** formation



3. **Only specific T lymphocytes has receptors with the complementary shape to antigen will be activated**
   → **Clonal selection**

4. T cell divides by **mitosis**
   → **Clonal expansion**

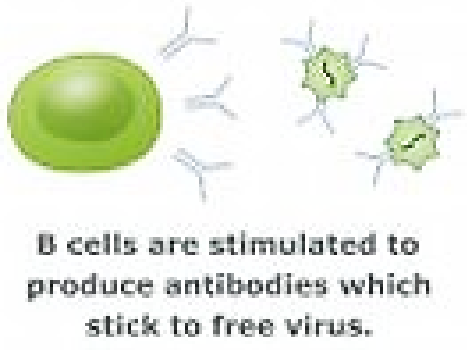
5. Activated T cells develop into **T helper cells** and **T killer cells**



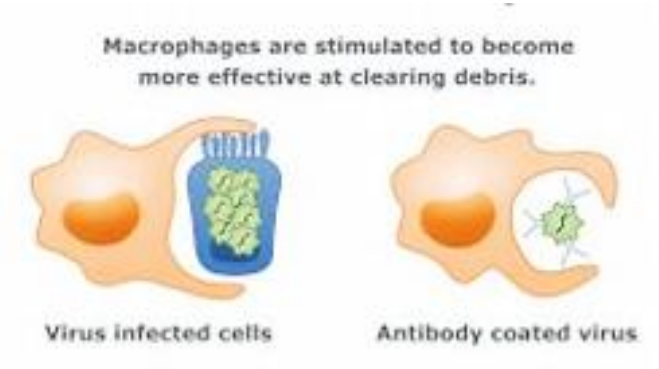
T Helper Cells

Functions:

1) Secrete **cytokines** / interleukins which….



a) **Stimulate** specific **B cells**
   - To divide and develop into **plasma cells & memory B cells**
   - Increased **antibody levels**



b) **Stimulate macrophages**
   - To carry out phagocytosis more vigorously

c) **Stimulate killer T cells**
   - To divide and produce more toxins

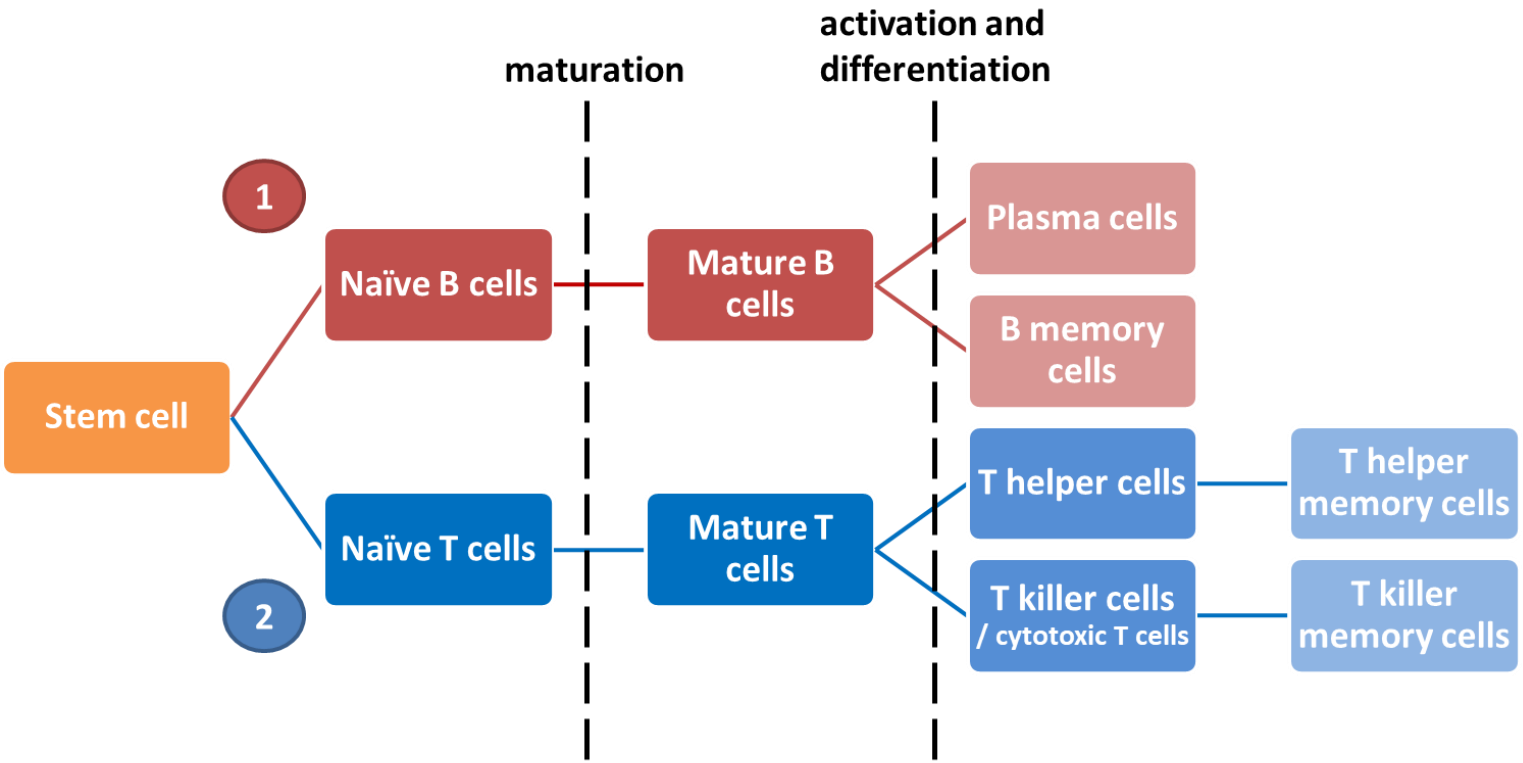
2

T Helper Cells

Functions:

2) Form T helper **memory cells**

- Secondary response
- Long term immunity



Cytotoxic T Killer Cells

Functions:

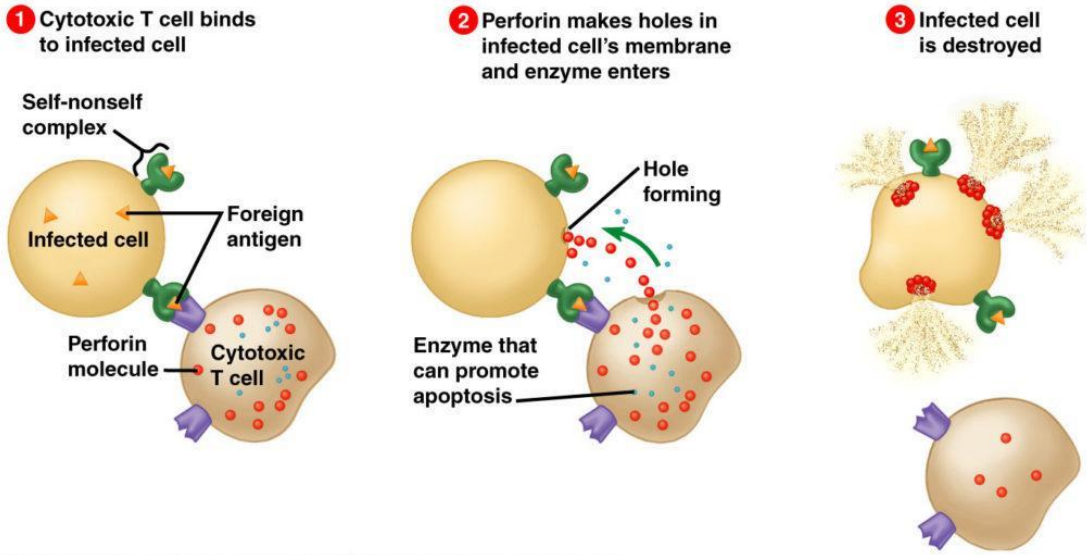
1) Seeks out **infected host cells** (including APC, cancer cells) and pathogens and **destroys** them

a) Attach to surface of cells

b) 'Punch' holes into cells

c) Secrete toxins into cells

- **E.g. hydrogen peroxide, perforin**


1 Cytotoxic T cell binds to infected cell
Self-nonself complex
Infected cell
Foreign antigen
Perforin molecule
Cytotoxic T cell
2 Perforin makes holes in infected cell's membrane and enzyme enters
Hole forming
Enzyme that can promote apoptosis
3 Infected cell is destroyed

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https://www.youtube.com/watch?v=ntk8XsxVDi0

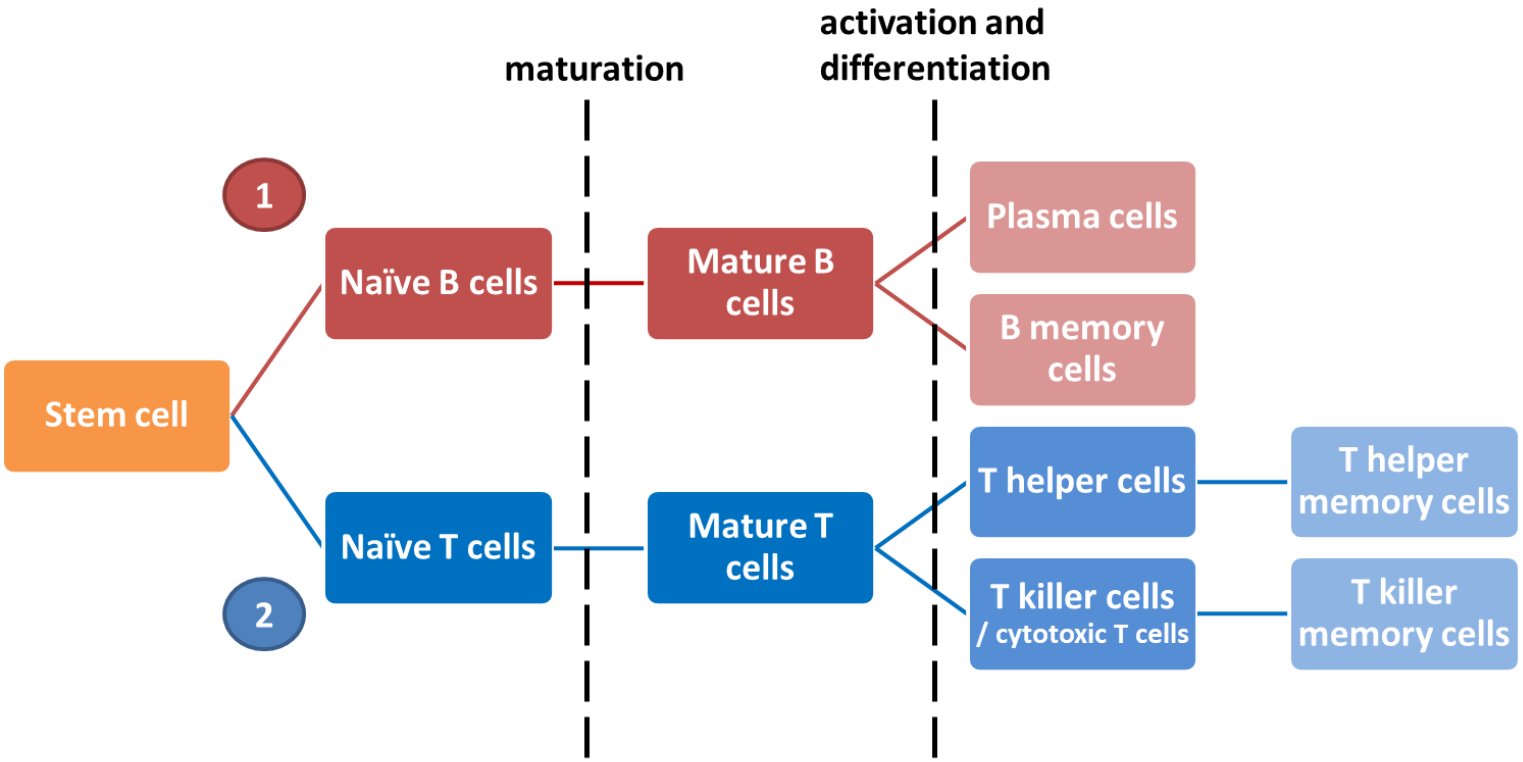
2

Cytotoxic T Killer Cells

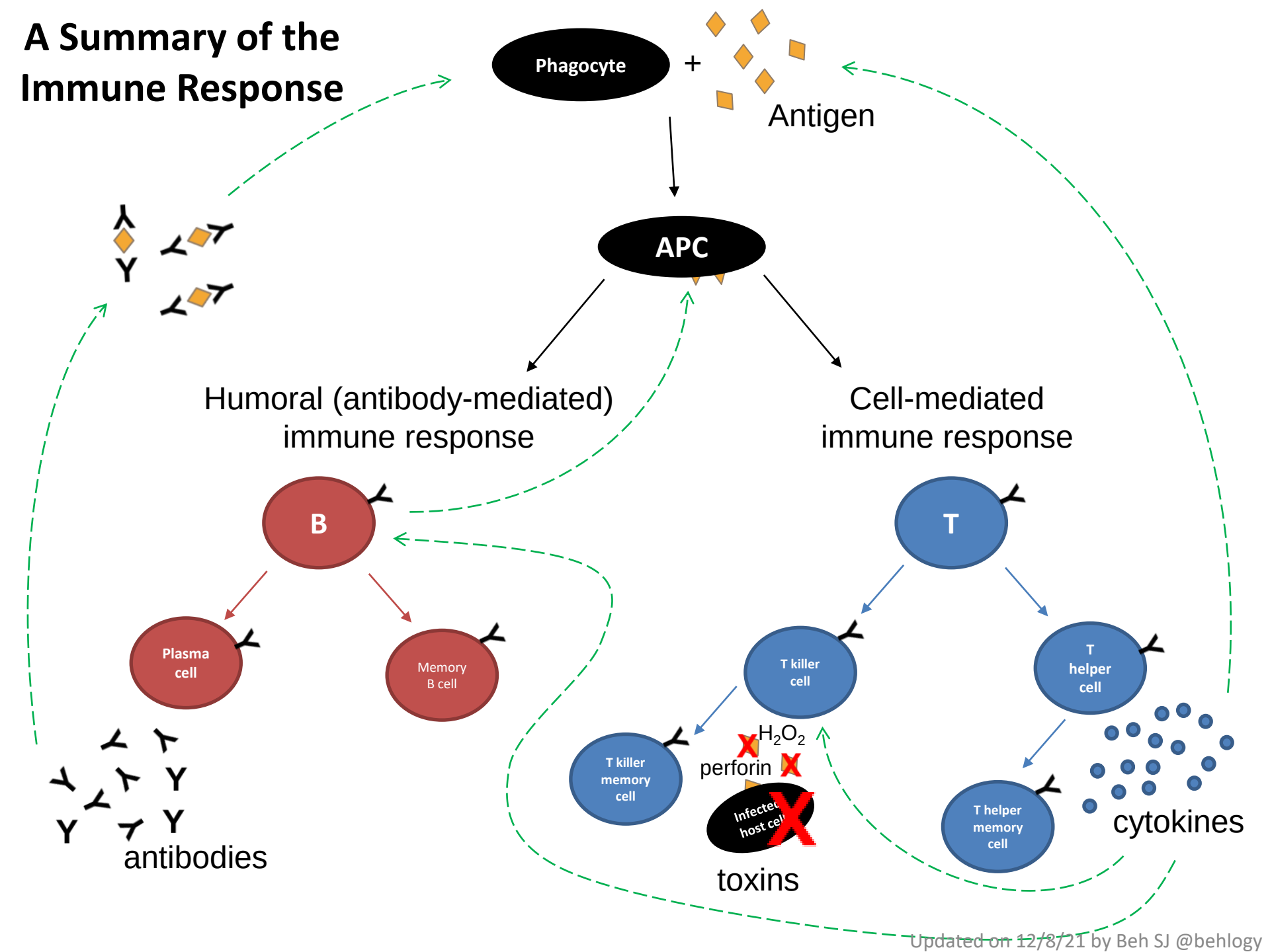
Functions:

2) Forms killer T **memory cells**

- Secondary responses
- Long term immunity as it is long-lived

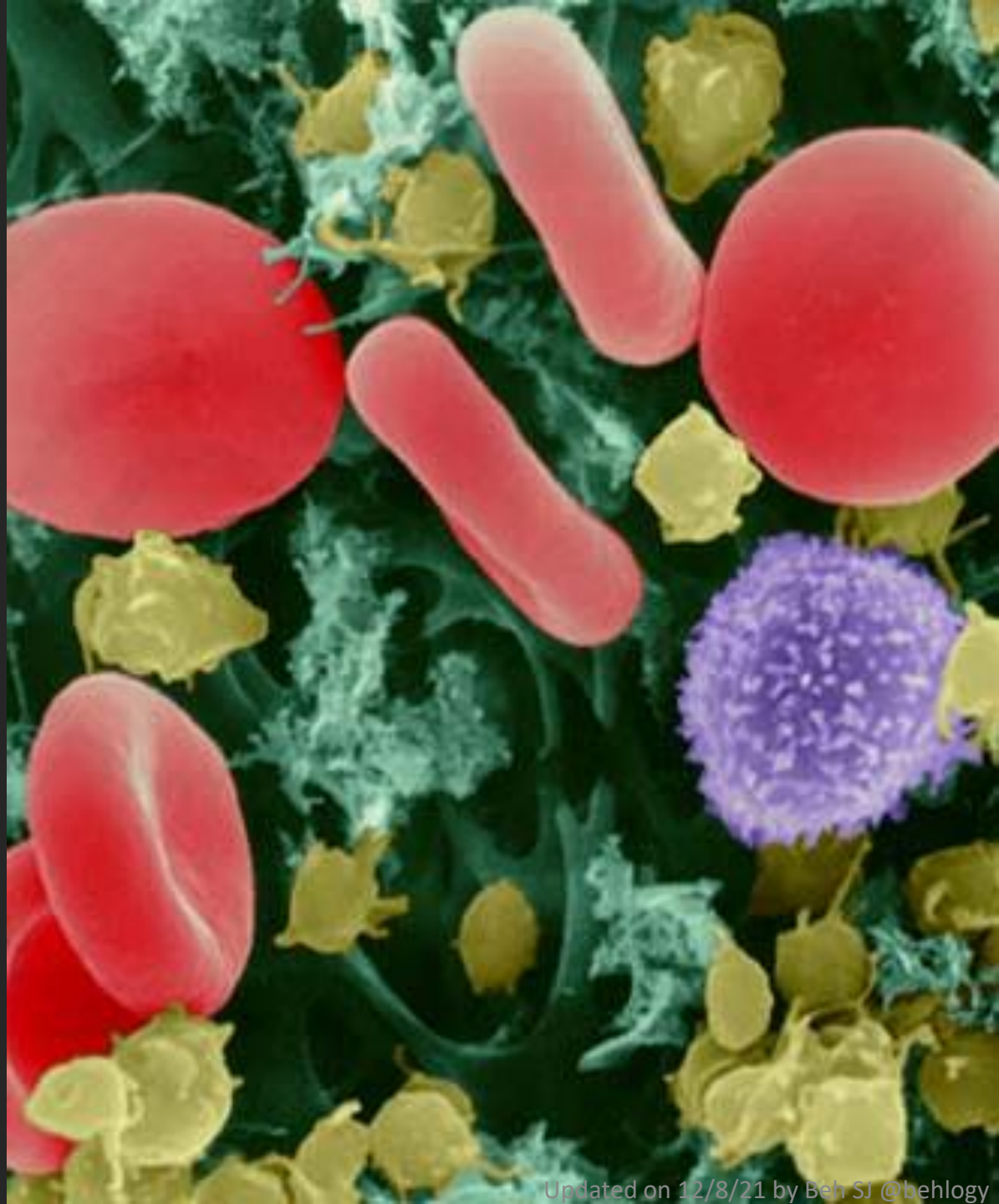


A Summary of the Immune Response



Chapter 11 (Part 2)

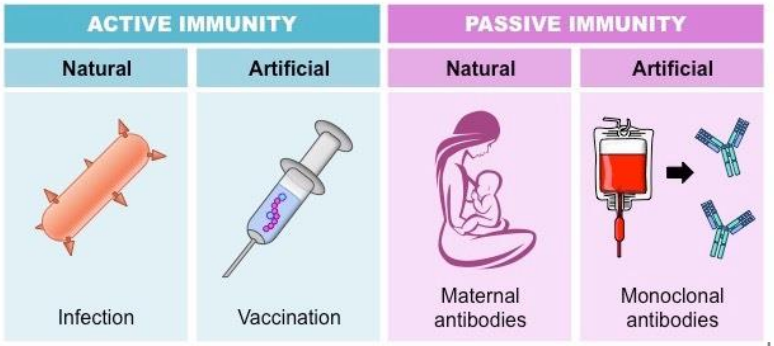
Vaccination and Monoclonal Antibodies

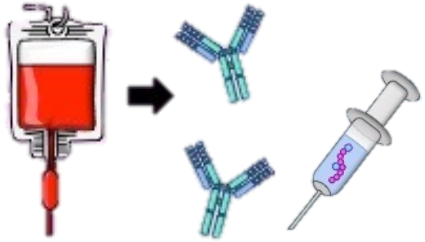


Types of Immunity

- **Active:** Own immune response is **activated**
  - Own **lymphocytes** are activated by antigens
  - Own **antibodies** are made
  - Takes time, not immediate
  - **Memory cells** formed → results in ***long-term immunity***

- **Passive**: Immune response is **NOT activated**
  - Own lymphocytes cells not activated
  - NO plasma cells to produce antibodies
  - Protection is immediate
  - NO memory cells formed → only ***short-term immunity***





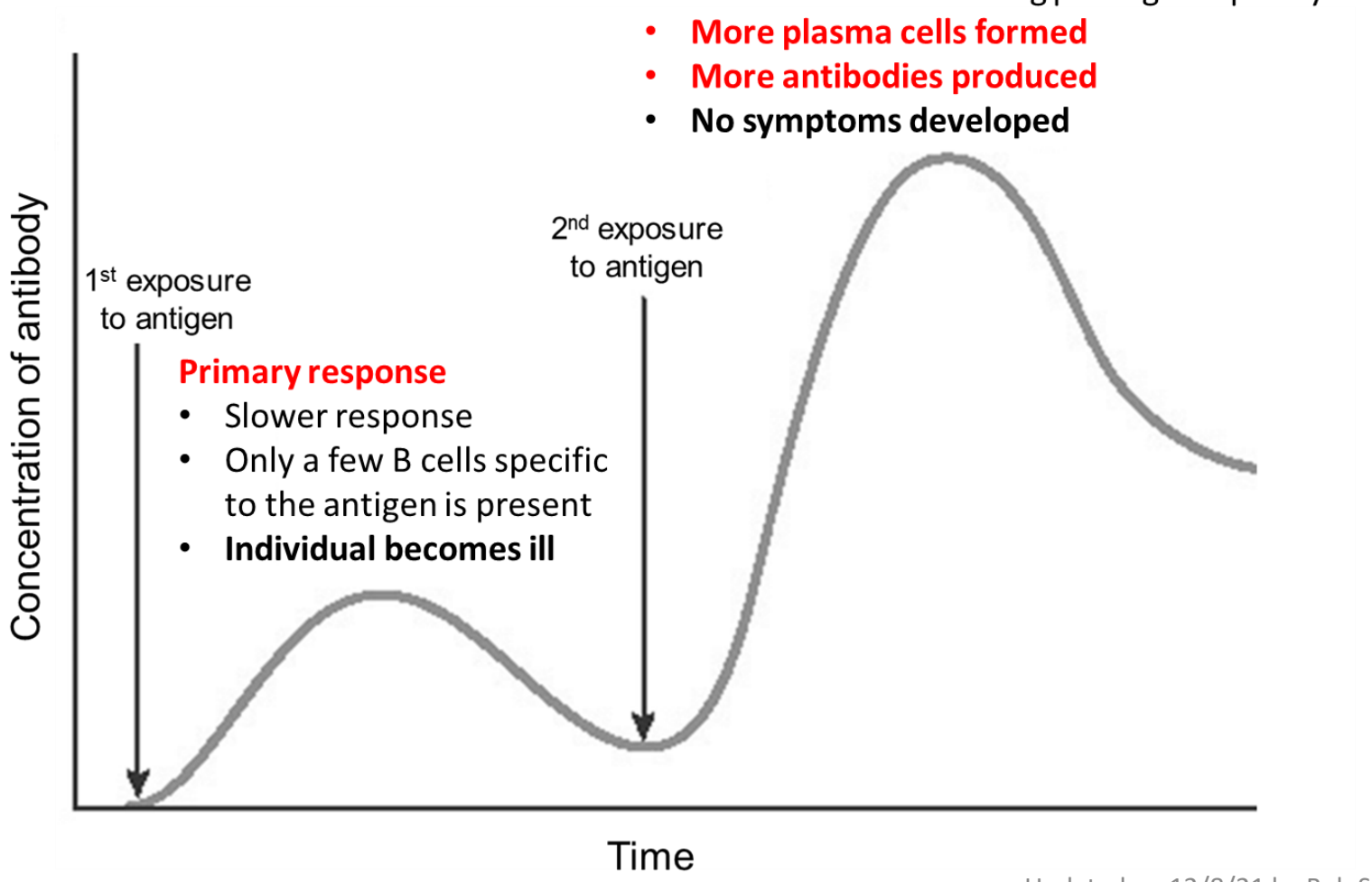
Active Natural Immunity	Active Artificial Immunity	Passive Natural Immunity	Passive Artificial Immunity
E.g. Catching a cold **Natural**: Antigens from the environment	E.g. **Vaccination** **Artificial**: Antigens are introduced via injection into vein or muscle / consumed → activate the immune response artificially Antigens can be **attenuated** / made harmless (e.g. heat-treated, cut up, inactivated toxins) Antigen used could be dead or alive	E.g. **Maternal antibodies** **Natural**: 1) Antibodies pass from mother to infant through **placenta** → remain for months 2) **Breast milk** that is colostrum-rich has antibody (IgA) that prevents growth of bacteria/viruses in the stomach of infant	E.g. **Antibodies or antitoxins** **Artificial**: Antigens are introduced via injection Antibodies are collected from blood of donor / animals who are vaccinated or suffer from the same disease → Contains the specific antibodies against the specific antigen

Active Natural Immunity

Antibody Levels after Infection

Secondary response

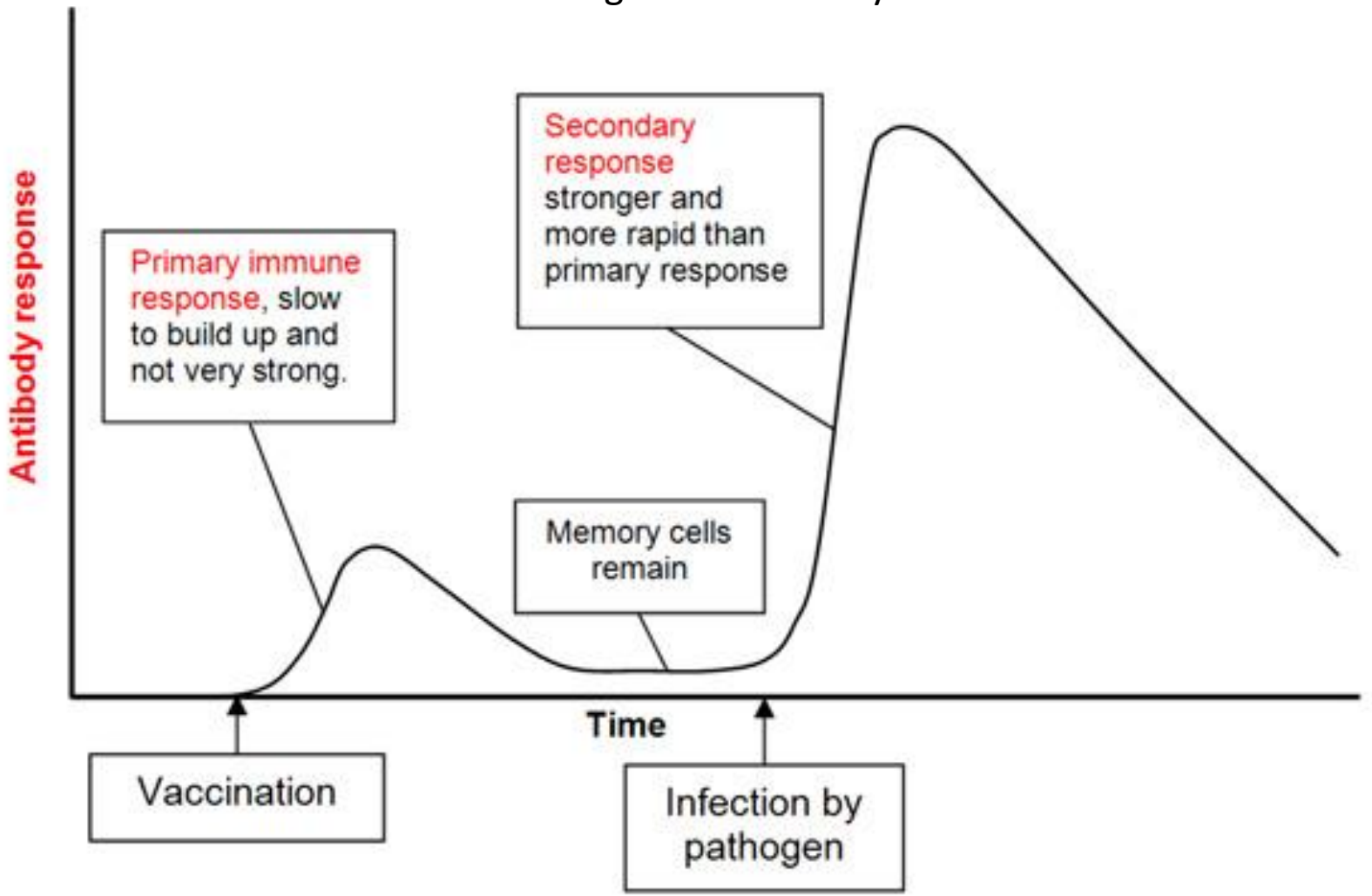
- **Faster response**
- Many memory cells circulating
- More cells specific for pathogen, higher chance of encountering pathogens quickly
- **More plasma cells formed**
- **More antibodies produced**
- **No symptoms developed**


Concentration of antibody
1st exposure to antigen
2nd exposure to antigen
Primary response
• Slower response
• Only a few B cells specific to the antigen is present
• Individual becomes ill
Time

Active Artificial Immunity

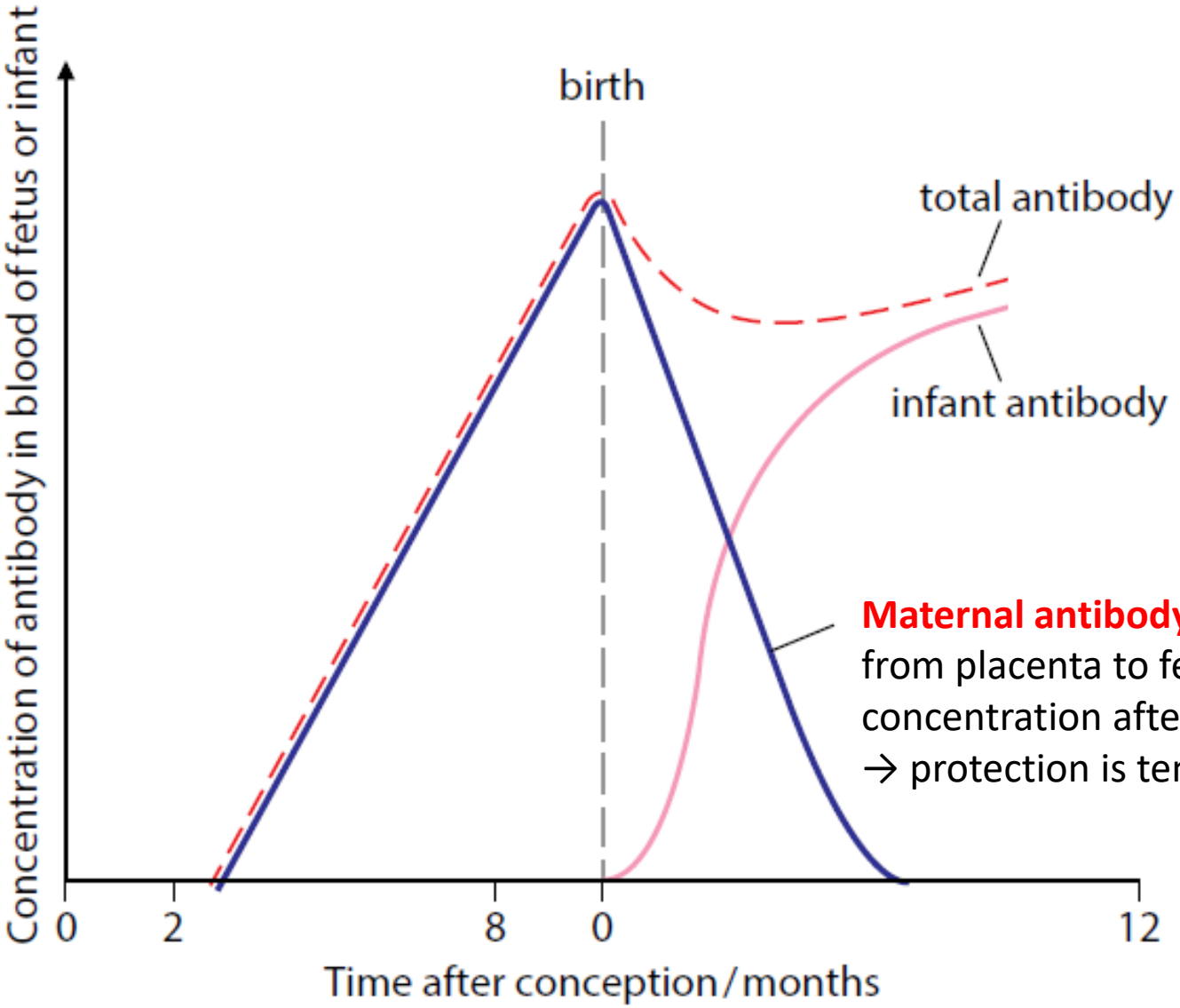
Antibody Levels after Vaccination

Vaccination activates the immune system → producing memory cells that result in long term immunity

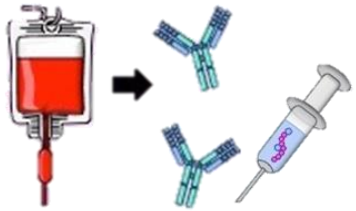

Antibody response
Primary immune response, slow to build up and not very strong.
Secondary response stronger and more rapid than primary response
Memory cells remain
Time
Vaccination
Infection by pathogen

Passive Natural Immunity

Antibody Levels in the Blood of Fetus or Infant

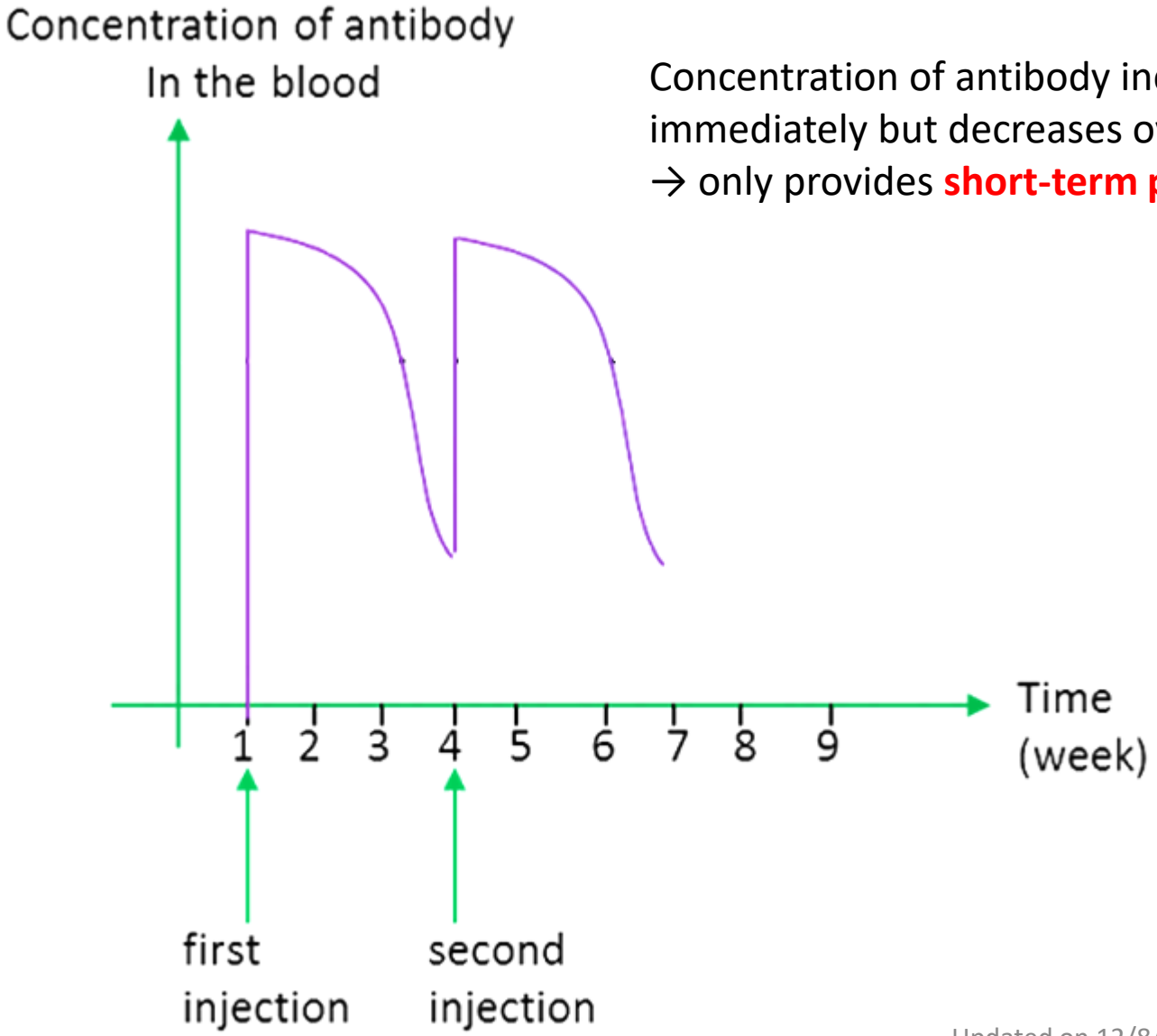


Maternal antibody passed from placenta to fetus drops in concentration after birth
→ protection is temporary



Passive Artificial Immunity

Antibody Levels after Antibody Injection



Concentration of antibody increases immediately but decreases over time
→ only provides **short-term protection**

Vaccination

Effective Vaccines	Ineffective Vaccines
Provide sufficient antigens → To mimic or copy natural infections → To form sufficient plasma and memory cells for long-term protection	Do not mimic natural infections → No plasma and memory cells formed
Give lifetime protection against pathogen → Pathogen unable to developed in immunised person	Do not give lifetime protection → Require booster injections → To stimulate secondary response in order to give protection Do not provide sufficient protection against pathogen → Maybe due to pathogen's high mutation rate or ability to hide from immune system
E.g. vaccines using live pathogens, smallpox vaccine	E.g. vaccines using dead pathogens, cholera vaccine

Vaccination

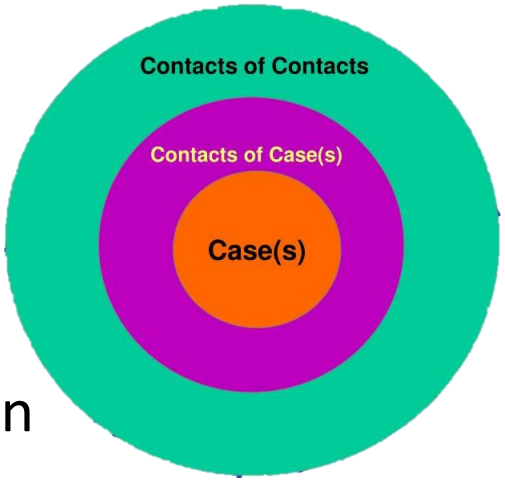
Two modes:

1. Mass vaccination

- Vaccinate a large number of people at the same time

2. Ring vaccination

- Perform **contact tracing** with infected person
- Vaccinate the area of community the person is in / people who was in contact with the person



- **Aim: Vaccinate a high proportion of the population**

→ To achieve herd immunity

Herd Immunity

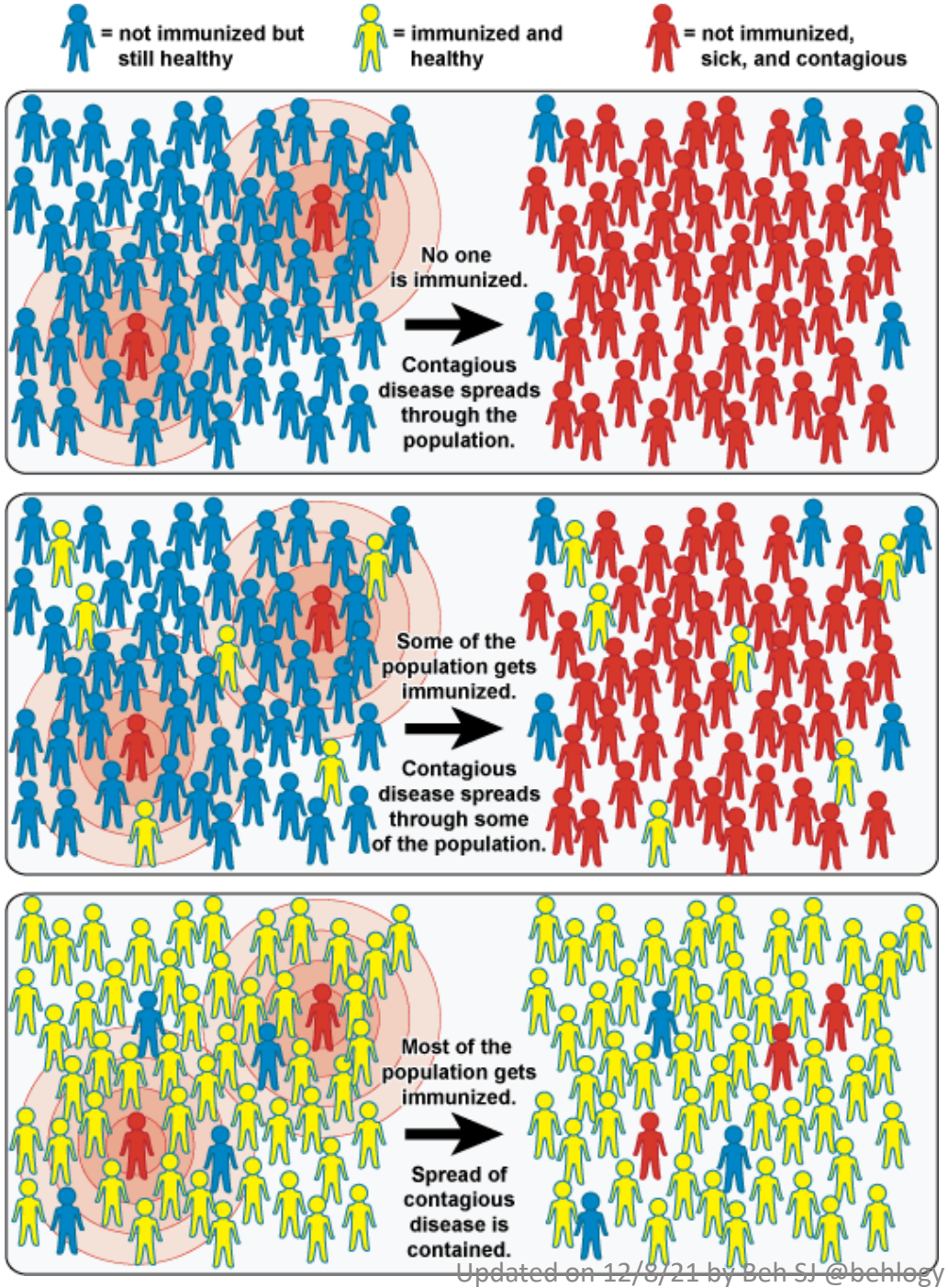
- Mass vaccination results in in **herd immunity**

- **Less chance of transmission** of disease

→ Reduce pool of infected people in the community

→ Fewer people can catch the disease and be source of infection

- **Protection of those unvaccinated / immunocompromised** as disease does not spread


= not immunized but still healthy
= immunized and healthy
= not immunized, sick, and contagious
No one is immunized.
Contagious disease spreads through the population.
Some of the population gets immunized.
Contagious disease spreads through some of the population.
Most of the population gets immunized.
Spread of contagious disease is contained.

Common Barriers to Vaccination

1) Poor response to vaccines

- People that are **immunocompromised**

- People who **lack protein** (malnutrition)
- Less antibodies made

2) Pathogens can mutate rapidly (antigenic variation)

- Form diff strain with diff antigens
- Memory cells are unable to recognise pathogen that has major changes in antigen structure

3) Pathogens can escape from immune system (antigenic concealment)

- By living inside cells / covering bodies with host proteins / suppressing immune system

How was **smallpox** eradicted?

An effective vaccine was developed!
https://www.youtube.com/watch?v=yqUFy-t4MlQ

- Same vaccine used everywhere

→ *Variola* virus – stable, **low mutation rate**

- Use **live virus** so strong immune response

→ similar *Vaccinia* virus

- One dose enough to give life-long immunity, **no boosters needed**

- Vaccine is **heat stable**
- **Easy to administer**

→ Use bifurcated needle

→ Needle can be sterilized and reused

How was **smallpox** eradicated?

Mass vaccination was very successful!

This is due to:

- **High percentage of population immunized**

→ **Low cost** needed to for mass production of vaccine

→ Many volunteers became vaccinators

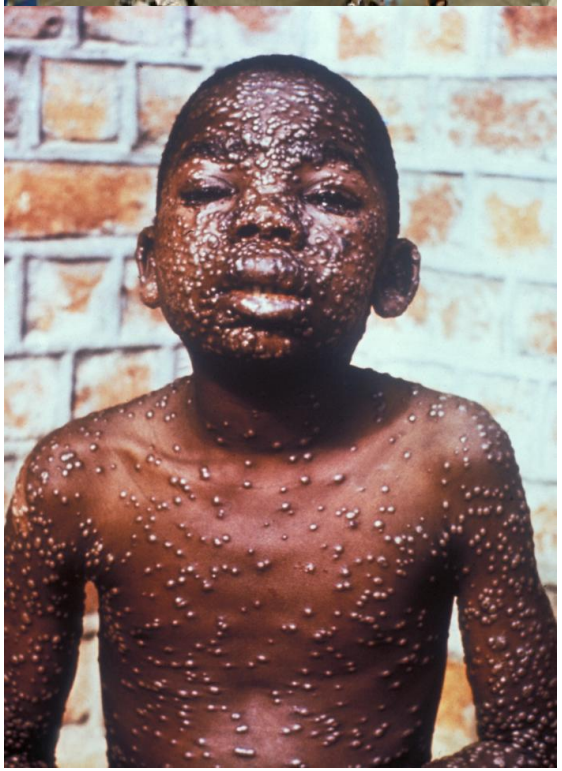
→ Result in **herd immunity**

- Infected people were **easy to identify**

→ Few symptomless carriers

→ Can perform contact tracing and **ring vaccination**

→ Can isolate cases to prevent spread



Why isn't **TB** eradicated already?

- BCG vaccine is available!
- It is not eradicated even though there is a high coverage of vaccination!

Why?

- Vaccination does not work in adults >35yo

- **High percentage cover (above 90%) needed to achieve herd immunity**

→ Not yet done in every country

- **Difficult for surveillance / to ensure vaccination**

→ Due to high birth rates and **high migration rates**

→ **Latent TB is symptomless** and found in 1 in 4 people

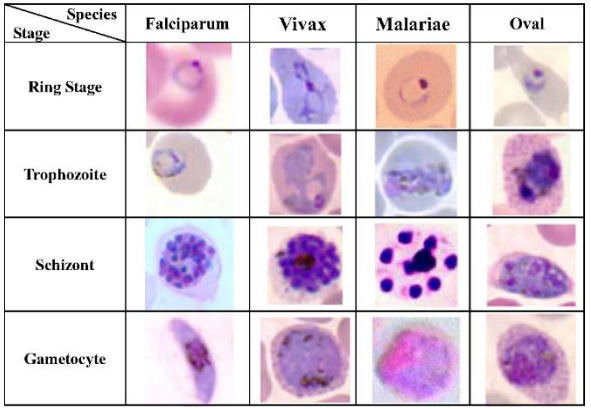
Why can't we vaccinate against **malaria**?

- No effective vaccines against malaria

Why?

- Protoctists are eukaryotes

→ **Many more genes** than bacteria & viruses



- Display **diff antigens** on its cell surface for:

→ **Diff species / strains**

→ **Different stages of its life cycle**

- Parasite **changes antigens during infection**

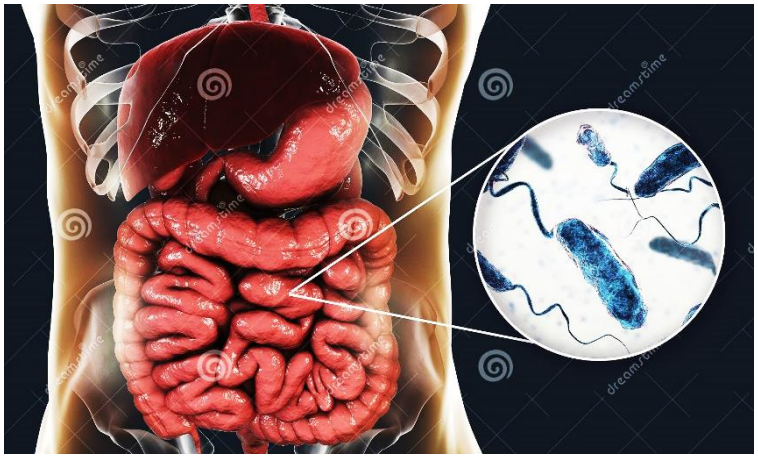
→ Diff genes coding for antigens switch on during infection

- *Plasmodium* parasite **hides in liver and RBCs**

Why can't we vaccinate against **cholera**?

- No effective vaccines against cholera
- Oral vaccination only gave limited protection as it was excreted

Why?



- Many different **strains** of cholera

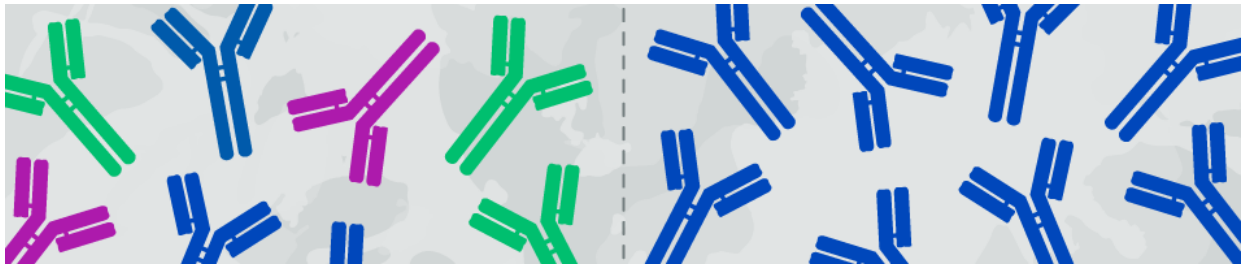
→ Bacterium mutates

- *Vibrio cholerae* lives in the **host's intestines**

→ Beyond reach of antibodies

Monoclonal Antibodies (Mabs)

- **Monoclonal** = only 1 type of antibody, **specific for 1 antigen**

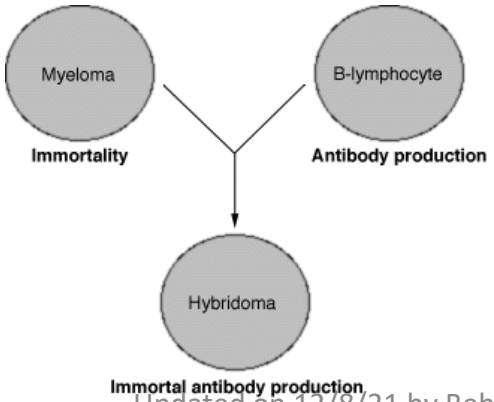


Problem:

- B cells that divide by mitosis **DO NOT produce antibodies**
- Plasma cells that secrete antibodies **DO NOT divide**

Solution:

Fuse **plasma cells + cancer/myeloma cells** → **hybridoma cells** that **CAN divide and CAN produce antibodies**



Monoclonal Antibodies (Mabs)

How to produce?

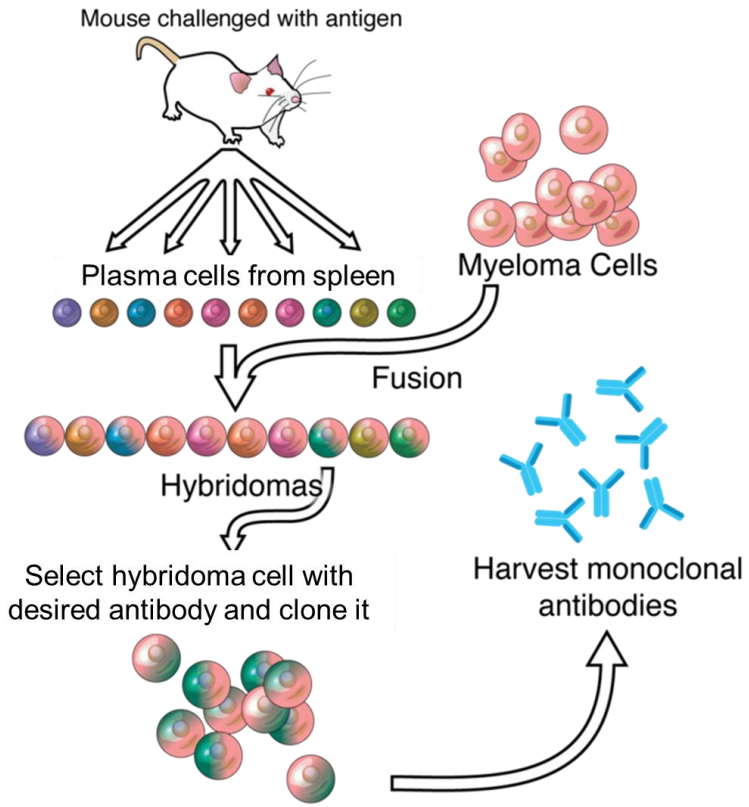
1) **Inject foreign antigen** (e.g. pathogen) into mice

2) Allow time for immune response to occur

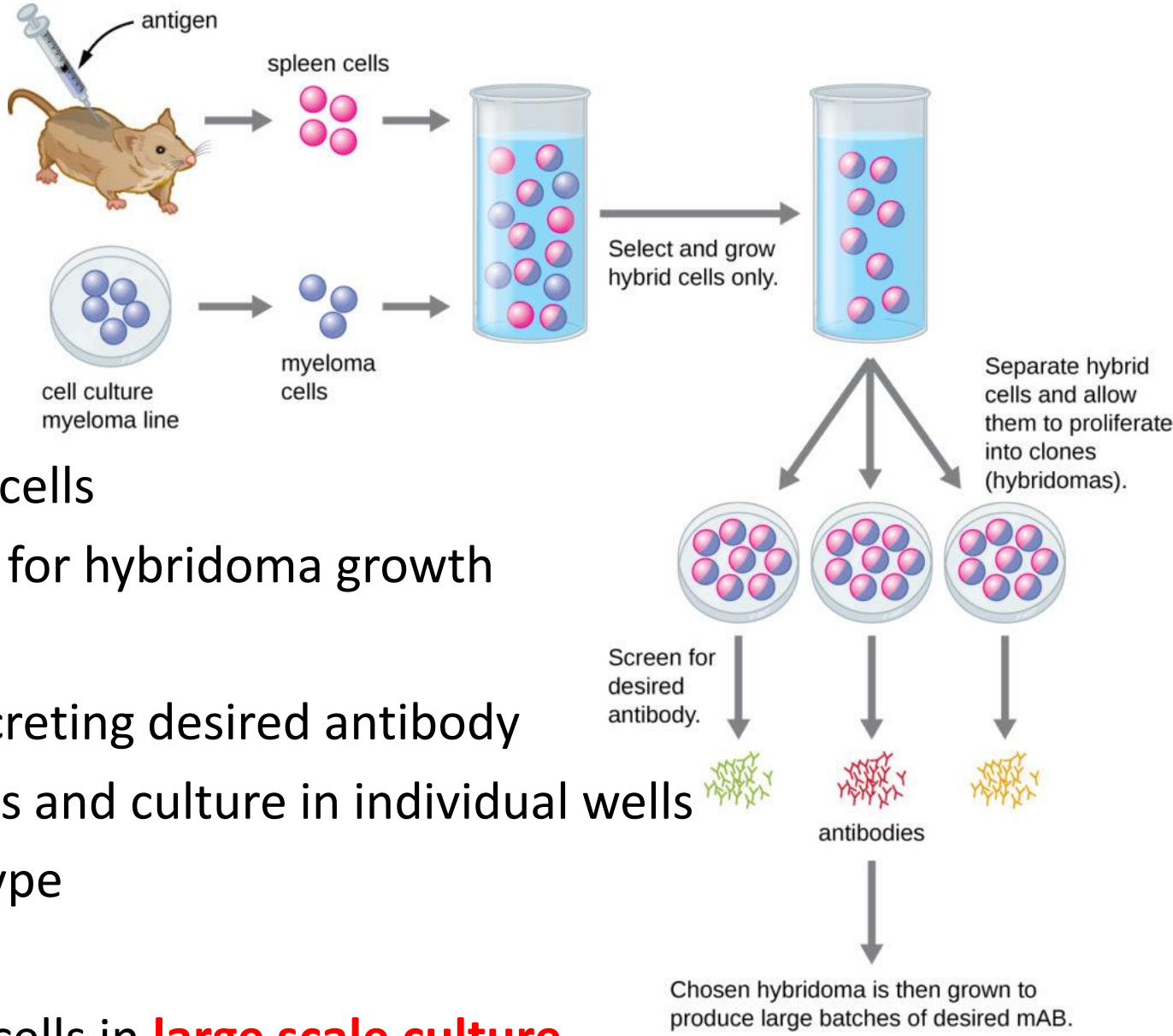
3) Collect **plasma cells** from **spleen**

3) **Fuse plasma cells with cancer cells** to produce **hybridoma cells**

→ Use fusogen for fusion



Monoclonal Antibodies (Mabs)



4) **Clone** hybridoma cells

→ Use HAT medium for hybridoma growth

5) **Screen** for cell secreting desired antibody

→ By separating cells and culture in individual wells

→ Select only one type

6) Grow hybridoma cells in **large scale culture**

Usage of Mabs

1) Diagnosis

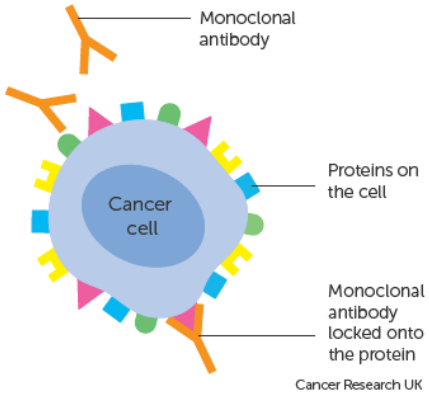
- Monoclonal antibodies have same specificity and detects only one antigen

→ Can **distinguish between diff pathogens / strains**

→ **Fast** diagnosis than having to culture pathogen

→ Less labour intensive

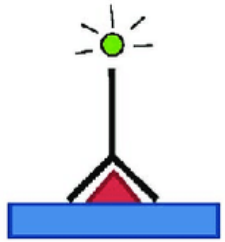
→ Quicker diagnosis = quicker treatment



- Can be **tagged with a fluorescent label/dye**

→ Can **detect location** of tissues expressing antigen

→ E.g. cancer cells, blood clots



- **Cheap, safe, fast results, easy to use, accurate**

(Also used in blood typing, pregnancy tests etc.)

Usage of Mabs

2) Treatment

- Used to **target specific diseased cell** by binding to **receptors** on its cell surface

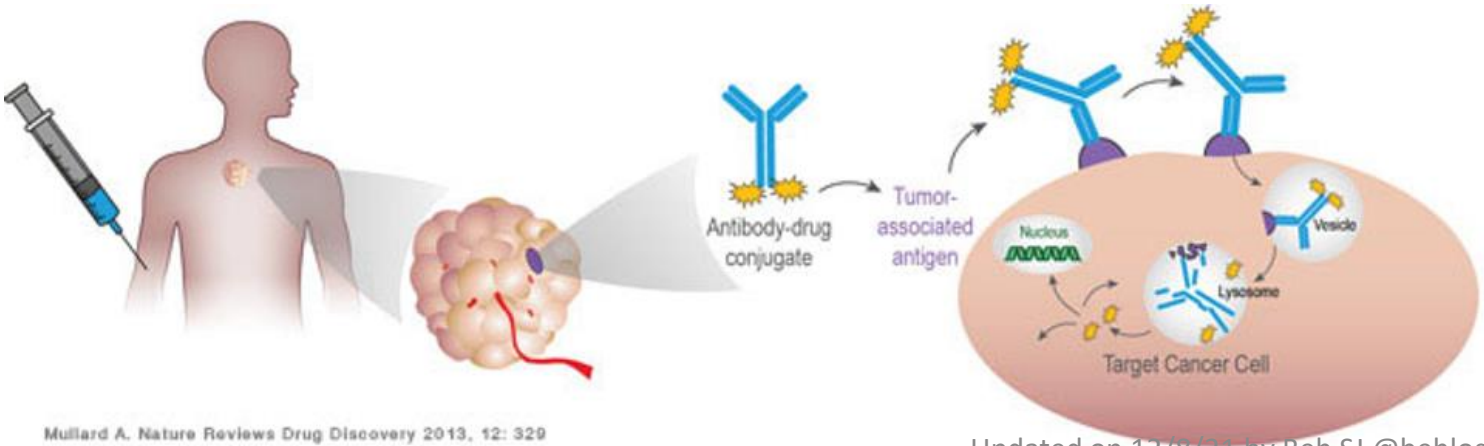
→ Can kill cell by **stimulating the immune system**

→ Can attach radioactive substance / drug to Mabs to kill cell

- Can bind to antigens on pathogens

→ Result in **artificial passive immunity**

E.g. Herceptin, Mab used to treat breast cancer



Mullard A. Nature Reviews Drug Discovery 2013, 12: 329

Problems of using Mabs in Treatment

Problems:

- Causes some side effects
- Antibodies made in animals **recognised as non-self**
- Trigger immune response in humans

→ **Allergic reaction**

- Remains in the body for **short period of time** as it is destroyed
- Need to be administered more than once in small amounts

Problems of using Mabs in Treatment

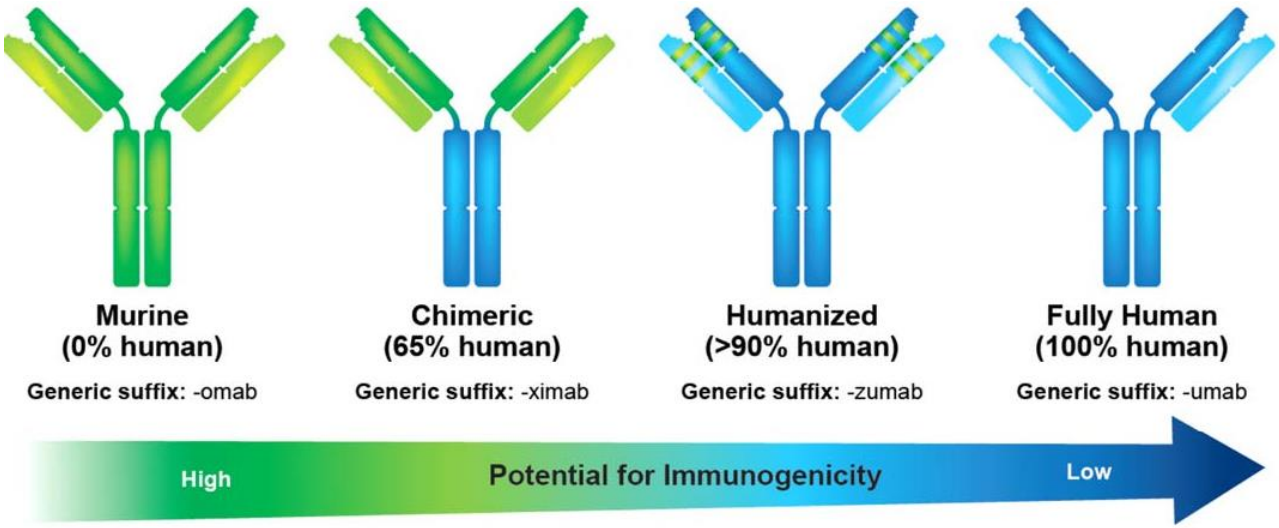
Solution: **Humanise Mabs**

1) **Alter genes** that code for heavy and light chains of antibodies

→ Code for human antibodies instead of mice and rabbit's

2) Changing **type and position of sugar groups** attached to heavy chains

→ Arrangement of sugar groups same as human antibodies



Example names of Mabs:

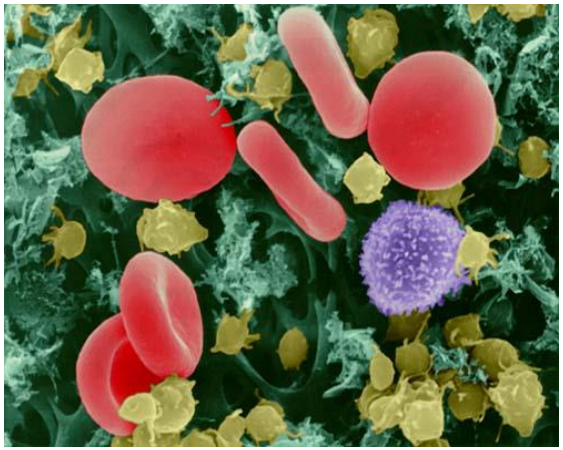
- Infliximab
- Rituximab
- Ipilimumab

P/S: No need to memorise details of diagram or Mabs names lah

Chapter Outline

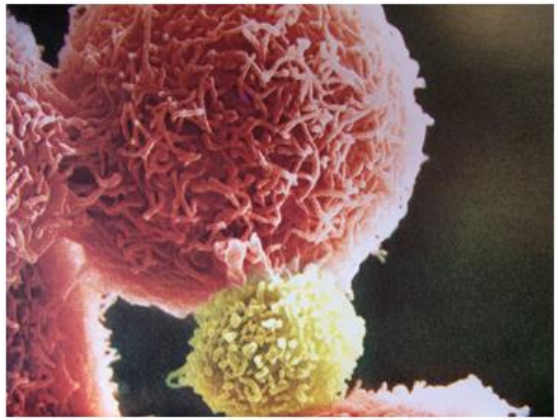
Part 1: The Immune Response

- Definitions: Immune response, antigen, self and non-self
- **Phagocytes**
  - Antigen presentation
- **B-lymphocytes**
  - Antibodies: structure and function
  - plasma cells and memory cells
- **T-lymphocytes**
  - T helper cells and T killer cells



Part 2: Vaccination and Monoclonal Antibodies

- Active vs Passive // Natural vs Artificial Immunity
- **Vaccination**
  - How smallpox was eradicated
  - Why vaccines aren't effective for other diseases
- **Monoclonal antibodies**



Videos! (again, warning – some of these things are not in your syllabus)

B-lymphocytes

- https://www.youtube.com/watch?v=JnXxU5XAVWU

T-lymphocytes

- https://www.youtube.com/watch?v=WdCiaIS2LV4

TED-Ed: How does your immune system work? - Emma Bryce

- https://www.youtube.com/watch?v=PSRJfaAYkW4

TED-Ed: Why it's so hard to cure HIV/AIDS

- https://www.youtube.com/watch?v=0TipTogQT3E

How do Pregnancy Tests Work?

- https://www.youtube.com/watch?v=aOfWTscU8YM